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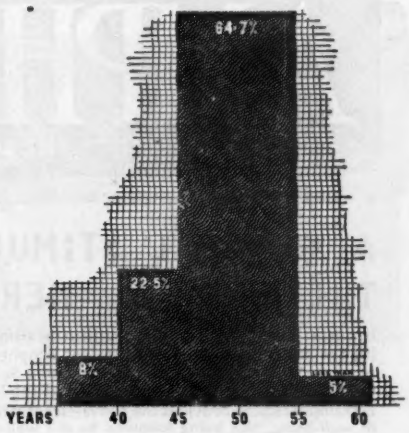

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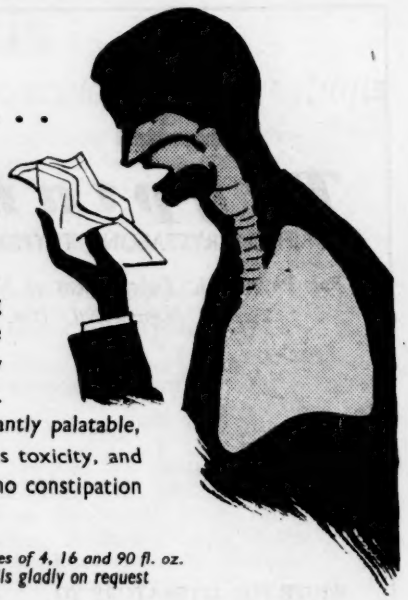

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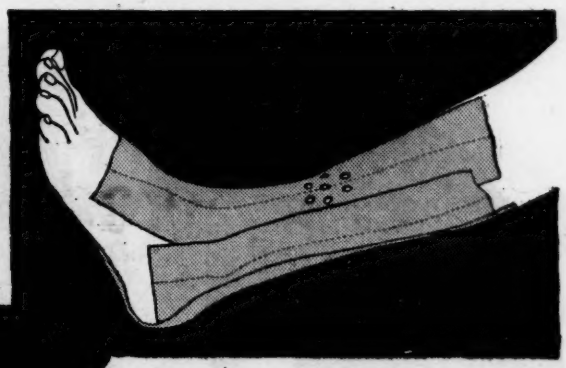

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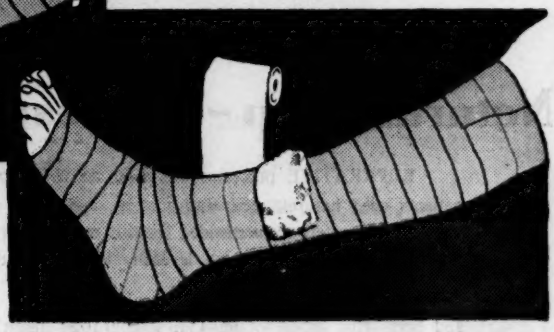
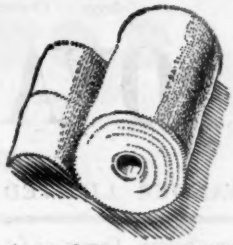


Cotton wool, held in place over holes by a further strip of Elastoplast, absorbs discharge. See illustration opposite.

Elastoplast TRADE MARK

POROUS ADHESIVE BANDAGES B.P.C.

The Elastoplast Bandage with Porous Adhesive complies with the B.P.C. It provides firm adhesion, compression and support while permitting free evaporation of skin exudates. Full details from Smith & Nephew Ltd., Welwyn Garden City, Herts., the marketing organisation of T. J. Smith & Nephew Ltd., Hull.



Outside the British Commonwealth, Elastoplast and Elastocrepe are known as Tensoplast and Tensocrepe respectively.

Natural sleep – the best ally

REPARATIVE processes are most active during the hours of sleep. When patients need natural, recuperative sleep, and when narcotics are contra-indicated, 'Ovaltine' may be safely recommended for this reason: it provides palatable, concentrated nourishment in a form which is easily absorbed without disturbing the patient's tranquillity.

'OVALTINE' contains only the best of natural foods—malt, milk, cocoa, soya and eggs—plus added vitamins in standardized quantities. It is therefore useful in the dietary management of those diseases which are complicated by insomnia. It engenders a warm, soothing feeling which helps to create the conditions most favourable to the best kind of sleep. 'Ovaltine' can be recommended with confidence.

OVALTINE

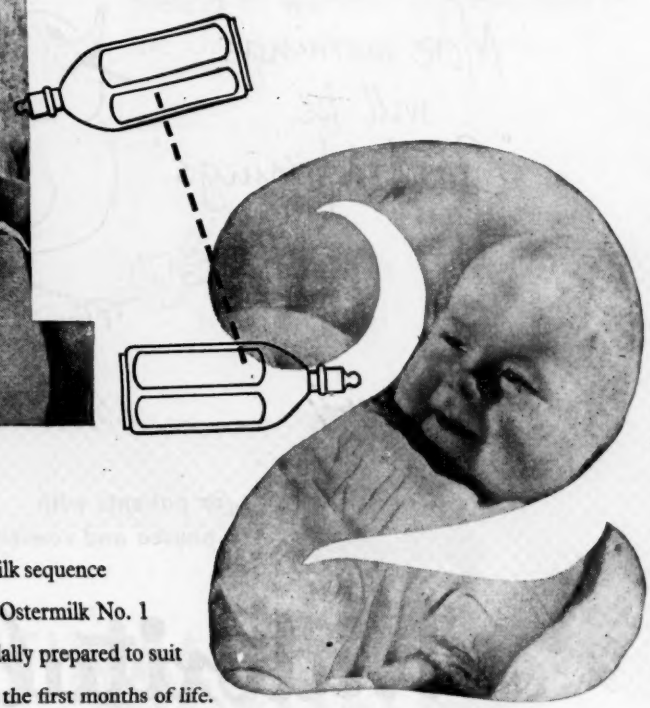
Vitamin Standardization per oz.—Vitamin B_1, 0.3 mg.; Vitamin D, 350 i.u.; Niacin, 2 mg.

A. WANDER LIMITED, 42 Upper Grosvenor Street, London W.1

Manufactory, Farms and 'Ovaltine' Research Laboratories: King's Langley, Herts.

M.382

SAFETY IN NUMBERS



From 1 to 2—that is the Ostermilk sequence for smooth *safe* bottle feeding. Ostermilk No. 1 is a fat-modified milk food specially prepared to suit the baby's digestive capacity in the first months of life. Ostermilk No. 2 is designed to meet 'growing needs' from the time the infant weighs 10 to 12 lb. The first 'Ostermilk children' are now men and women in their middle twenties, and a second generation of sturdy babies is bearing tribute to the value and reliability of Ostermilk. As a supplement to breast milk, or as a complete replacement, Ostermilk has set irreproachable standards of *safety, digestibility and nutritional value.*

OSTERMILK

NO 1 FAT-MODIFIED

NO 2 FULL-CREAM

Both foods contain added iron and vitamin D

IN 1-LB. TINS

GLAXO LABORATORIES LTD., GREENFORD, MIDDLESEX BYRon 3434

. . . for patients with
nausea and vomiting of pregnancy

Nidoxital CAPSULES

provide rapid and prolonged relief

In bottles of 12, 20 and 100 capsules.
Dosage: One capsule 30 to 45 minutes before meals. 20 capsules are usually sufficient for complete control.

LITERATURE ON REQUEST

each capsule contains:

Pyridoxine Hydrochloride	50 mgm
dl-Methionine	100 mgm
Nicotinamide	25 mgm
Benzocaine	100 mgm
Pentobarbital sodium	15 mgm

Ortho Pharmaceutical Limited

Ortho

HIGH WYCOMBE · BUCKINGHAMSHIRE · ENGLAND

"... generally after the first application there follows a feeling of warmth, improvement in the circulation and relaxation."*

* Pro medico 21, 429-431 (1952)

FINALGON OINTMENT

tube of 20 g

COMPOSITION:
Nonylic acid vanillylamide 0.4% and Nicotinic acid-β-butoxyethyl ester 2.5% in a suitable ointment base

produces a pleasant feeling of warmth lasting for hours and relieves rheumatic pains

LEWIS LABORATORIES LTD., LEEDS 9

The ideal nasal decongestant

Prompt Effect	Prolonged Action
Low surface tension—readily absorbed by the mucosa.	The prompt, sustained effect of Fenox gives prolonged relief with small dosage.

Non-Oily	Viscous
Fenox does not interfere with ciliary action and there is no danger of lipoid pneumonia.	Fenox has the same viscosity as mucus and remains at the site of action.

Non-Irritant	Non-Toxic
Fenox is *p*H-adjusted and isotonic with the nasal secretion.	Free from undesirable side effects—suitable for children and adults.

FENOX
NASAL DROPS

For the treatment of catarrhal conditions

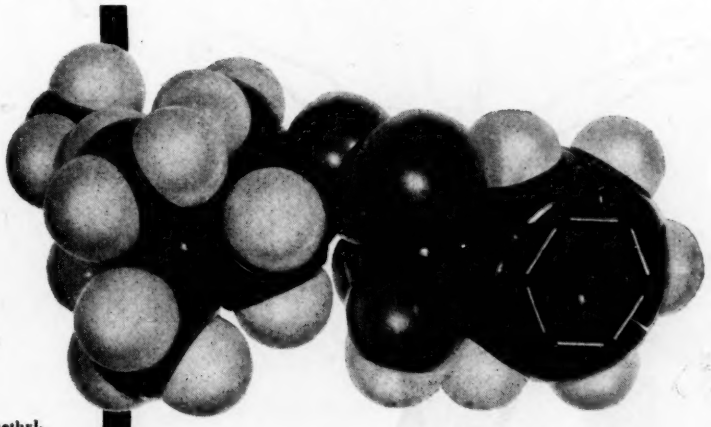
FENOX, the only preparation containing phenylephrine hydrochloride and naphazoline nitrate, marks an advance in the local treatment of catarrhal conditions of the nasal passages and accessory sinuses. It exhibits all the properties of the ideal nasal decongestant.

The advantages of FENOX are available at low cost—it is supplied in ½ fl. oz. dropper bottles—Retail Price 2/6d, subject to usual discounts.

Literature and "Patients' Directions" pads are available from the Medical Department, Boots Pure Drug Co. Ltd. Nottingham.

Boots

3192



mandelic
acid
ester
of
3.5.5-trimethyl-
cyclohexanol

CYCLOSPASMOL

(CYCLOMANDOL) BS 572*

Clinical investigations carried out in several parts of the world as reported in the medical press have established CYCLOSPASMOL as a very effective vasodilator in the treatment of peripheral vascular diseases.

Due to its low toxicity there is a complete absence of undesirable side effects.

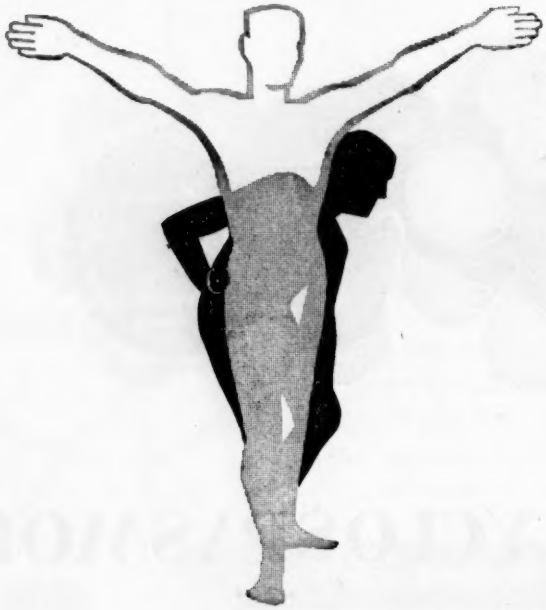
* *protected by patents e.q. patent applications*

BROCADES

N.V. KONINKLIJKE PHARMACEUTISCHE FABRIEKEN V/H
BROCADES-STHEEMAN & PHARMACIA
AMSTERDAM - THE NETHERLANDS

150 YEARS OF EXPERIENCE AND VIGILANT RESEARCH

The Rheumatic Patient-a New Approach



The new approach consists of a combined attack by the three components of the formula—mephenesin, which abolishes skeletal muscle spasm; salicylamide, a new and reliable analgesic in rheumatic conditions; with homatropine methylbromide, to prevent or diminish the gastro-intestinal upsets which so often accompany rheumatic disorders.

MEPHOSOL is a real contribution to the problem of pain in rheumatism.

Each tablet contains	Mephenesin	125 mg.
	Salicylamide	250 mg.
	Homatropine methylbromide	$\frac{1}{8}$ mg.

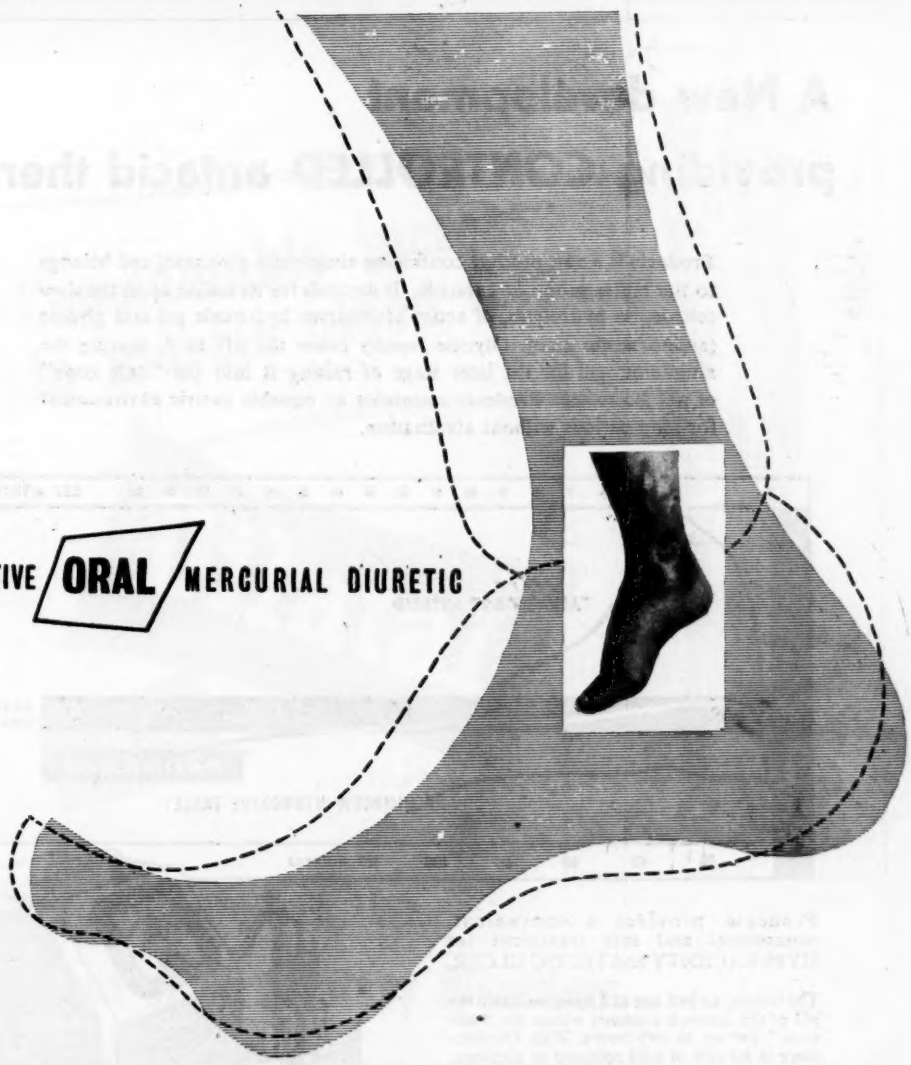
The average dose is 2-3 tablets every 3 or 4 hours.

Supplied in bottles of 25 and 100 tablets.

CROOKES MEPHOSOL

Registered Trade Mark

THE CROOKES LABORATORIES LIMITED · PARK ROYAL · LONDON N.W.10



AN EFFECTIVE **ORAL** MERCURIAL DIURETIC

Effective diuretic therapy by oral administration is now made possible by MERCLORAN. One tablet three times daily, equivalent to 30 mg. mercury, is usually sufficient to keep cardiac patients free from oedema. Where more intensive treatment is needed MERCLORAN, being well tolerated by the majority of patients, can be taken more often and in increased doses. The need for injection is thus frequently eliminated.

In severe cases, it is often desirable to initiate *treatment parenterally, in which case the chemically related compound MERCARDAN (meralluride Sodium U.S.P.) is available.*

MERCLORAN

(CHLORMERODRIN N.N.R.)

IN BOTTLES OF 25 AND 250 TABLETS

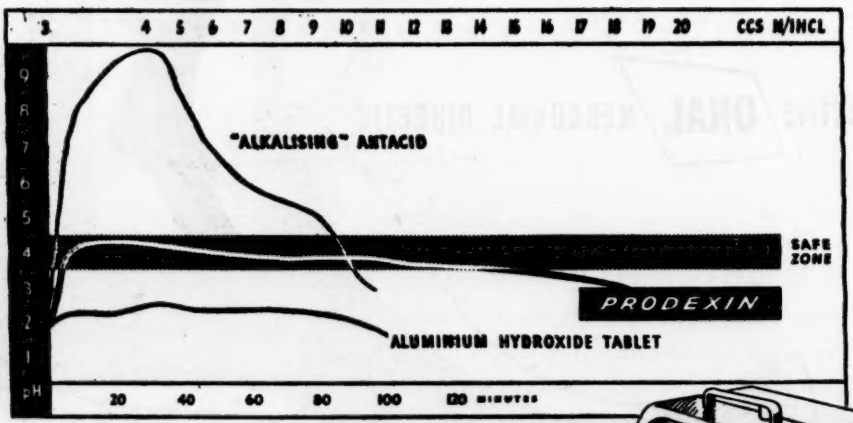
AND **MERCARDAN** FOR PARENTERAL USE

PARKE, DAVIS & COMPANY, LIMITED *(Inc. U.S.A.)* HOUNSLOW, MIDDLESEX. Telephone: Hounslow 2361 570

*K 15

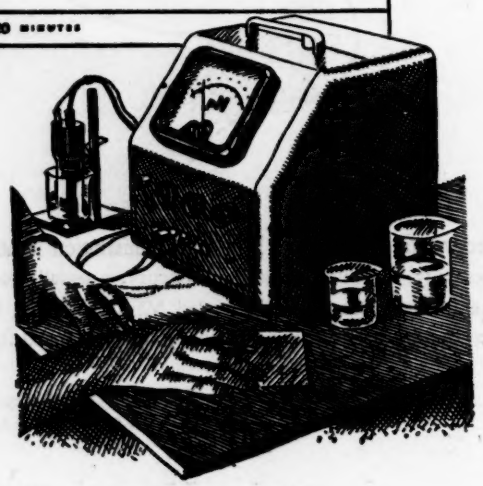
A New development providing CONTROLLED antacid therapy

Prodexin is a new product containing aluminium glycinate, and belongs to the buffer group of antacids. It depends for its action upon the slow release, on hydrolysis, of active aluminium hydroxide gel and glycine (amino acetic acid). Glycine rapidly raises the pH to 2, sparing the aluminium gel for the later stage of raising it into the "safe zone" of pH 3·5 to 4·5. Prodexin maintains an equable gastric environment for long periods without alkalisation.


3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 CCS N/10HCL
9 8 7 6 5 4 3 2 1 pH
"ALKALISING" ANTACID
SAFE ZONE
PRODEXIN
ALUMINIUM HYDROXIDE TABLET
20 40 60 80 100 120 MINUTES

Prodexin provides a convenient, economical and safe treatment for HYPERACIDITY and PEPTIC ULCER.

The tablets, sucked one at a time, maintain the pH of the stomach contents within the "safe zone" for up to two hours. With Prodexin there is no risk of acid rebound or alkalosis. Prodexin tablets are pleasant to suck and they do not form gritty particles in the mouth or give rise to constipation.



PRODEXIN

Each tablet contains:—

Aluminium glycinate.....0·9 gramme.
(*dihydroxy aluminium aminoacetate*)
Light magnesium carbonate.....0·1 gramme.

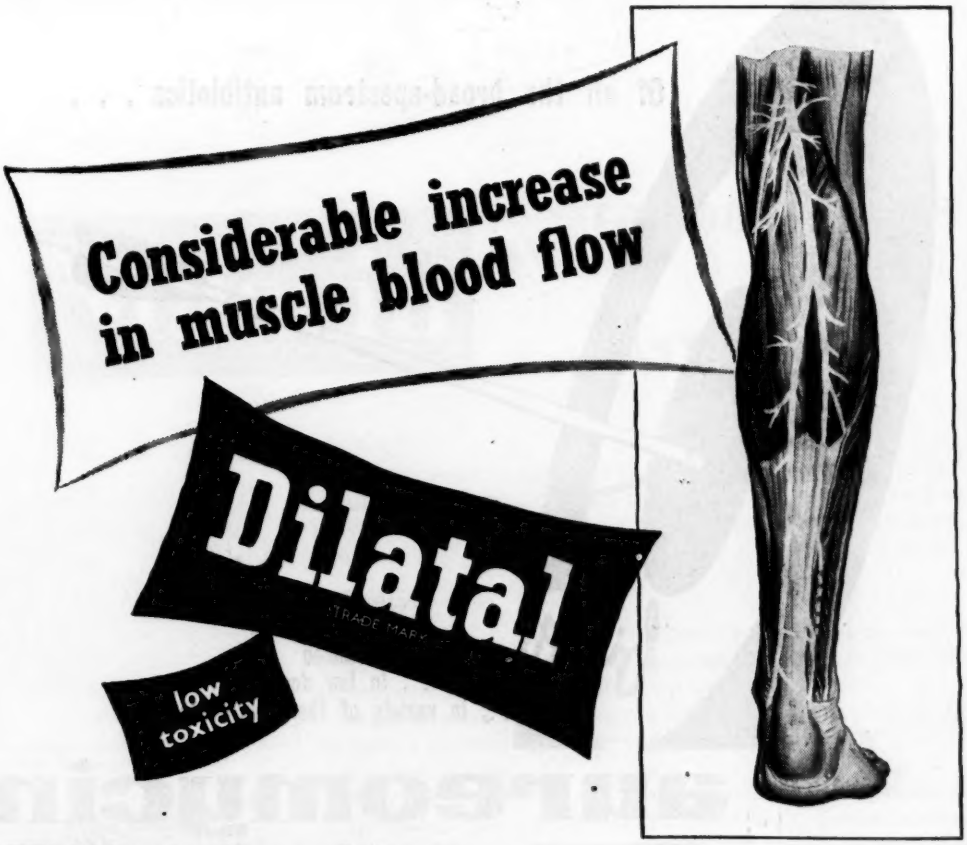
The basic N.H.S. cost of treatment at the rate of 6 Prodexin tablets daily is 8½d.

Manufactured in the laboratories of

C. L. BENCARD LIMITED

MINERVA ROAD · PARK ROYAL · LONDON N.W.10

BENCARD



Widely indicated in the treatment of circulatory disorders

- INCREASED CARDIAC OUTPUT MAINTAINS MEAN ARTERIAL PRESSURE.
- DIRECT ACTION ON THE MUSCULATURE OF THE BLOOD VESSELS.

DILATAL* is safe and rapidly effective by oral and parenteral administration. Available in tablets (2.5 mg. in containers of 100 and 500) and ampoules (5 mg. in 1 ml.—in boxes of 12).

*1-(p-hydroxyphenyl)-2-(1'-methyl-3'-phenyl-propylamino)-propanol-(1) hydrochloride

SMITH & NEPHEW LTD.,
WELWYN GARDEN CITY, HERTS.,
the marketing organisation of Herts Pharmaceuticals Ltd.,
the manufacturers and owners of the trade mark DILATAL.

GM160

Of all the broad-spectrum antibiotics . . .

first . . to be introduced
. . in low dosage
. . in variety of therapeutic forms

aureomycin
Lederle

for potency • safety • economy

Aureomycin is the original and true low-dosage broad-spectrum antibiotic which is universally recognised by leading authorities for its effectiveness and wide range of action. It combines potency with safety and economy, and has been acclaimed the antibiotic of choice in a vast array of infections of bacterial, rickettsial, large viral and unknown aetiology.

It is available in the following forms :—

Capsules	Ointment	Soluble Tablets
Dental Cones	Ophthalmic Ointment	SPERSOIDS* Dispersible Powder
Dental Paste	Ophthalmic	Troches
Intravenous	Otic	Vaginal Powder
Nasal		

Detailed literature on request **Trade mark*

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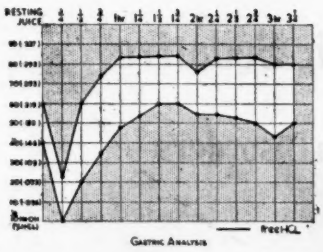
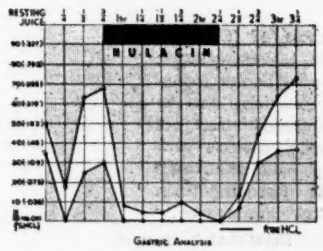
LEDERLE LABORATORIES DIVISION
Cyanamid Products Ltd.
BUSH HOUSE · ALDWYCH · LONDON, W.C.2 · TEMPLE BAR 5411

Nulacin

FOR CONTROL OF GASTRIC ACIDITY



Superimposed grue. fractional test-meal curves of five cases of duodenal ulcer



Same patients as in Fig. 1, two days later, showing the striking neutralizing effect of sucking Nulacin tablets (3 an hour). Note the return of acidity when Nulacin is discontinued.

NULACIN provides control of gastric acidity comparable with that obtained with intragastric milk-alkali drip therapy. It is the most convenient and effective form of treatment for bed and ambulatory patients.

DOSAGE

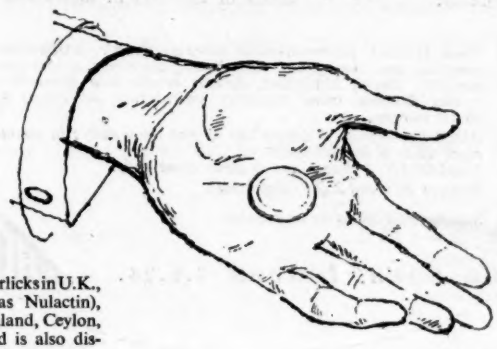
A NULACIN tablet, placed in the mouth and allowed to dissolve slowly, releases its contained medicaments at a rate that gives continuous neutralization of the gastric juice.

NULACIN tablets are indicated whenever neutralization of the gastric contents is required: in active and quiescent peptic ulcer, gastritis, gastric hyperacidity.

Beginning half an hour after food, a NULACIN tablet should be placed in the mouth and allowed to dissolve slowly. During the stage of ulcer activity, up to three tablets an hour may be required. For follow-up treatment, the suggested dosage is one or two tablets between meals.

NULACIN tablets are not advertised to the public and have no B.P. equivalent. May be prescribed on E.C.10. The dispensing pack of 25 tablets is free of Purchase Tax. (Price to pharmacists, 2/-.) Also available in tubes of 12.

NULACIN tablets are prepared from whole milk combined with dextrins and maltose, and incorporate Magnesium Trisilicate 3.5 grs.; Magnesium Oxide 2.0 grs.; Calcium Carbonate 2.0 grs.; Magnesium Carbonate 0.5 grs.; Ol. Menth. Pip. q.s.



NULACIN
is available from Horlicks in U.K., U.S.A., Canada (as Nulactin), Australia, New Zealand, Ceylon, Malaya, India, and is also distributed in most other countries

BIBLIOGRAPHY:

The Control of Gastric Acidity, 26th July, 1952, Brit. Med. J., 180-182

Medical Treatment of Peptic Ulcer, 27th February, 1952, Med. Press, 195-199

The Effect on Gastric Acidity of "Nulacin" Tablets, 28th November, 1953, Med. J. Aust., 823-824

Control of Gastric Acidity by a New Way of Antacid Administration, (1953), J. Lab. Clin. Med. 42:955

Further Studies on the Reduction of Gastric Acidity, 23rd January, 1954, Brit. Med. J., 183-184

Horlicks Limited
PHARMACEUTICAL DIVISION
SLOUGH, BUCKS.

NEW

Convenil REGD.

(PHENYLETHYLACETIC ACID - β - DIETHYLAMINOETHYLESTER CITRATE)

Antispasmodic-Sedative

in Autonomic Nervous System Disorders

'Convenil'-Hommel is an entirely new preparation, synthesized in the Swiss Laboratories of Hommel, which provides a highly effective antispasmodic action with excellent tolerability and freedom from side-effects.

'Convenil' is put up in convenient dragees, each containing 150 mg. of the new active agent. It thus obviates the induction of the hypnotic effects of the common antispasmodics, since it is a single-drug prescription and does not depend upon any barbiturate content for its efficacy.

Clinical experiences of **'Convenil'** prove its value in unblocking spasm in a wide variety of autonomic lesions including spastic functional disorder of the gastro-intestinal tract. In addition, 'Convenil' corrects peripheral vagosympathetic disturbance thus increasing the effect of soporifics. It is therefore a 'barbiturate saver'.

Investigations also show that 'Convenil' is useful in the management of postoperative spastic phenomena, neuroses and in the neurological side-effects of Isoniazid in tuberculosis.

INDICATIONS *These include: gastro-intestinal neuroses, spastic constipation, menstrual and menopausal disturbance, autonomic dysfunction generally, chronic alcoholism, nervous tension and irritability, cardiac dystonia, travel sensitivity, neurological side-effects of INAH therapy.*

DOSAGE *ADULTS: average 1 dragee two to four times daily; in special cases up to 6 dragees daily.*
CHILDREN: 1 dragee one to three times daily.

PACKINGS *Dragees 20's and 250's (dispensing).*

Samples and literature on request

HOMMEL, 121 NORWOOD ROAD, LONDON S.E.24.

HOMMEL

GM. 161

Lower toxicity with higher dosage in tuberculosis therapy

NUPASAL-213

(o-hydroxybenzal isonicotinyl hydrazone)

NUPASAL-213 is a new derivative of Isoniazid. First synthesized and studied in our laboratories (1), Nupasal-213 possesses high anti-tuberculous activity and is very much less toxic than Isoniazid. Experimental evidence (2) indicates it is active in cases of Isoniazid resistance because its lower toxicity permits higher dosage. American workers have reported a successful trial of this new drug (3) and clinical evaluation is under way in this country (4).

Nupasal-213 is now available for clinical use in tablets of 100 and 250 mg.

(1) J. Pharm. Pharmacol. 1952, 4, 844.
(2) Lancet, 1954, 2, 337.
(3) Trans. 13th Conference on Chemotherapy of Tuberculosis (Veterans Administration) Feb. 1954, p.374.
(4) Lancet, 1954, 2, 337.

SMITH & NEPHEW LTD.
WELWYN GARDEN CITY, HERTS.,
the marketing organisation of Herts Pharmaceuticals Ltd., owners of the trade mark NUPASAL-213.

Further information on request from Smith & Nephew Research Ltd., Hunsdon Laboratories, Nr. Ware, Herts. (Tel.: Stanstead Abbotts 234).

The complete treatment for

Vaginal Leucorrhoea

and

Vaginitis

Fundamentally, "Floraquin" aims to acidify the vagina and to destroy all offending organisms. "Floraquin" is non-arsenical, being a skilful combination of the potent protozoacide Diodoquin* with lactose, dextrose, and boric acid. It not only destroys pathogenic organisms but also brings the pH of the vagina to the desirable level of between 3.8 and 4.4. Thus, a favourable environment is furnished for the growth of the normal protective bacterial flora.

SEARLE

Floraquin* **TABLETS & POWDER**

brand of di-iodohydroxyquinoline compound

"Floraquin" therapy consists of insertion of two moistened "Floraquin" vaginal tablets high in the vaginal vault night and morning, supplemented by "Floraquin" powder insufflation twice or thrice weekly; treatment being continued through the menses.

"Floraquin" Powder is supplied in 1 oz. bottles (2.15 gm. Diodoquin* per ounce); "Floraquin" Tablets in boxes of 24 and in bottles of 400 (dispensing pack only) each tablet containing 100 mg. Diodoquin*.

**Diodoquin (Searle) is a non-toxic, insoluble, highly protozoacidal di-iodide of hydroxyquinoline.*

Literature on request.

*TRADE MARKS

SEARLE

Ethical Pharmaceuticals since 1888

G.D. SEARLE & CO., LTD.

17, Manchester Street
London, W.1.

Telephone: Welbeck 1306.

Penicillin

to meet the needs of General Practice

by mouth

Permapen*

tablets

STABLE—TASTELESS—ECONOMICAL

Pack of 18 foil wrapped scored tablets each 200,000 units

for children *and the elderly*

Permapen*.

oral suspension

PLEASANT TO TAKE — READY PREPARED

Bottles 60 ml.—300,000 units per large teaspoonful

by injection

Permapen

Plus*

FOR RAPID, PERSISTENT AND SUSTAINED ACTION

Single dose vials containing 600,000 units

Pfizer — *World's Largest Producer of Antibiotics*

VITAMIN-MINERAL FORMULATIONS
HORMONES

*Trade Marks

Full literature is available and will be supplied on request

PFIZER LTD · FOLKESTONE · KENT · tel: Folkestone 51771

HYDROCORTISONE
MADE IN ENGLAND
SKIN OINTMENT

CORTISONE
EYE OINTMENT

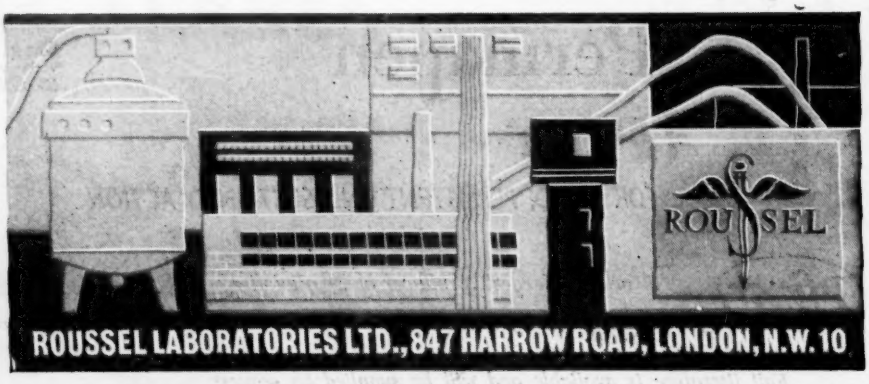
ROUSSEL

UNITED KINGDOM

Orders can now be accepted from Hospitals only, for HYDROCORTISONE SKIN OINTMENT AND CORTISONE EYE OINTMENT but not for other presentations, which are still distributed exclusively by the Ministry of Health

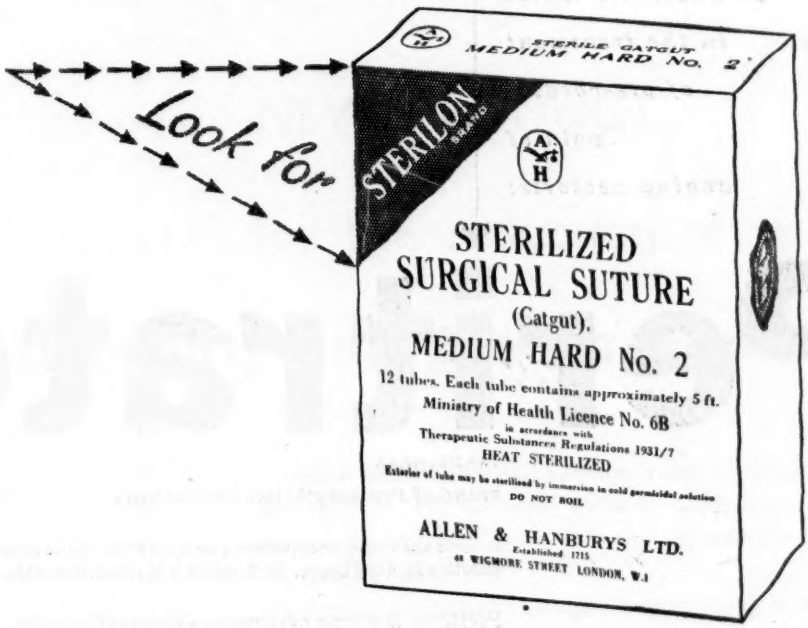
EXPORT

All forms of Hydrocortisone and Cortisone are freely available



ROUSSEL LABORATORIES LTD., 847 HARROW ROAD, LONDON, N.W. 10

For the *NEW* SEMI-MATT FINISH



STERILON CATGUT
has the NEW SEMI-MATT FINISH
to MINIMISE KNOT-SLIP.

STERILON CATGUT
IS UNAFFECTED BY AGE OR CLIMATE.

ALLEN & HANBURYS LTD LONDON E2
Makers of Quality Instruments
SHOWROOMS: 48 WIGMORE STREET LONDON W1

A new oral prophylactic tablet in the treatment of pre-cordial pain of angina pectoris:

Peritrate

TRADE MARK

brand of Pentaerythritol Tetranitrate

A coronary vasodilator, active ½ an hour after swallowing and effective for 4 to 5 hours. Each tablet is of 10 mg. strength.

Peritrate is a drug of considerable benefit in the prophylactic treatment of patients with coronary insufficiency, regardless of their age. The evidence of clinical trials indicates that in some cases Peritrate may protect completely against attacks; in others, the number of attacks is substantially reduced; while those attacks not prevented may be less intense and of shorter duration. Results so far obtained with Peritrate suggest that it is more efficacious than drugs such as aminophylline or khellin; also there are certain other beneficial effects which can be expected:

1. Less palpitation, especially at night.
2. Shortness of breath on effort, less severe.
3. An improvement of 50 per cent. in distance walked.
4. Reduction of nitroglycerin requirement.
5. The negative S-T segment shifts, ordinarily occurring after exercise, modified; Peritrate has returned the abnormal resting electro cardiogram towards normal in a significant number of cases.

DOSAGE 1 or 2 tablets (10 mg. or 20 mg.) 4 times daily.
PACKING AND PRICES Bottles of 50 and 500 tablets. Dispensing bottle of 500 tablets supplied to chemists at 9/- plus P.T. 2/3.

William R. Warner & Co. Ltd., Power Road, London, W.4

★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★

Announcing a

NEW PRODUCT

for the reduction of

Hypermotility and Gastric Secretion

★ ★

'Lergine' brand Tricyclamol Chloride, a new anticholinergic drug discovered at The Wellcome Research Laboratories, markedly reduces motility and spasm of the gastro-intestinal tract and diminishes secretion.

The principal indication for 'Lergine' is as an adjunct to the medical treatment of peptic ulcer, where it affords rapid relief from pain. It also provides most effective relief in spastic conditions of the intestinal tract, especially those affecting the colon.

The average dose of 'Lergine' is 50 to 100 mgm. (one to two compressed products) every four to six hours. 'Lergine' is issued in bottles of 100 and 500.*

'LERGINE'

TRICYCLAMOL CHLORIDE

BURROUGHS WELLCOME & CO. (THE WELLCOME FOUNDATION LTD.) LONDON

MAINTAINING
DAY TO DAY RHYTHM

When the even timing of normal peristalsis is interrupted, day to day regularity of rhythm may be restored effectively by the administration of I-so-gel.

This natural laxative has a smooth mechanical action which stimulates normal peristalsis. I-so-gel does not contain purgatives. I-so-gel is invaluable in the treatment of habitual constipation and is particularly suitable for elderly and convalescent patients and diabetics. It is also indicated in mucous colitis, dysentery, hæmorrhoids and intestinal flatulence. After the performance of colostomy, I-so-gel gives excellent results by solidifying the fæces.

I-SO-GEL

GRANULES

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PORTAL-SYSTEMIC ENCEPHALOPATHY

NEUROLOGICAL COMPLICATIONS OF LIVER DISEASE

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NERVOUS disorders have been induced in patients with liver disease by the administration of certain nitrogenous substances (Van Caulaert 1932, Kirk 1936, Phillips et al. 1952).

In this paper neurological complications arising spontaneously in patients with liver disease will be described with particular reference to deranged nitrogen metabolism. Evidence will be advanced that toxic nitrogenous substances passing from the portal vein to the systemic circulation—through a damaged liver, portal collateral channels, or both—can cause a diffuse cerebral disturbance sometimes culminating in hepatic coma.

Case-material and Methods

18 patients with liver disease and neurological signs are described. In 13, histological confirmation of the diagnosis was obtained.

Impairment of *liver function* was assessed as mild, moderate, or severe on the basis of history, physical examination, and serial hepatic-function tests including the bromsulphthalein test.

The *portal-systemic venous collateral circulation* was graded as extensive, moderate, or insignificant by physical examination, barium swallow, and œsophagoscopy. Additional evidence was provided by percutaneous trans-splenic venography (Atkinson et al. 1954) in 7 patients and at post-mortem examination in 8 patients.

Blood-ammonium was estimated by Conway's (1950) micro-diffusion technique, ammonium being expressed as ammonia nitrogen in microgrammes per millilitre of blood. Hepatic-vein catheterisation was used in 11 patients to compare ammonium levels in hepatic-vein and peripheral-vein blood after a standard 3 g. dose of ammonium chloride by mouth. These results will be discussed in detail elsewhere (White et al. 1954).

Electro-encephalograms were obtained from 8 patients. Other investigations included measurements of the level of blood electrolytes, glucose and urea in all patients, and routine analysis of the cerebrospinal fluid, including estimation of ammonia, in 7 patients.

The Neurological Disorder

The neurological complications exhibited by these patients suggest a common basis despite the varied ætiology and extent of the liver disease.

Clouding of consciousness, usually shown by extreme apathy and confusion, occurred in all patients and sometimes progressed to coma. The lapse into coma might be abrupt but more often the insidious evolution of mental confusion and apathy, or sometimes extreme. emotional lability, was the first sign of deterioration. Though varied by grimacing and blinking, facial expression became vacant, salivation increased, and speech was slow, slurred, and increasingly restricted to the repetition of a few irrational phrases. Simultaneously comprehension became clouded so that simple requests were obeyed with difficulty, if at all, and socially bizarre behaviour, exemplified by lack of restraint, nocturnal ramblings, and a peculiar tendency to evacuate bladder and bowels in inappropriate places created embarrassing situations.

The episodes commonly began in the late evening, were of variable duration, and might terminate at any stage, patients having no recollection of their actions. Recovery was often rapid, consciousness returning before other neurological signs abated. Variation from day to day and even from hour to hour was particularly pronounced in the group with persistent signs.

A disorder of the motor system was present in every patient. The most characteristic was "flapping" tremor, which was observed in 17 of the 18 patients. It was best demonstrated, with the patient's arms outstretched and fingers separated, as a series of rapid flexion-extension movements at the metacarpophalangeal and wrist joints, accompanied often by lateral movements of the digits. Sometimes arms, neck, jaws, protruded tongue, retracted mouth, and tightly closed eyelids were involved and the gait was rendered ataxic. Absent at rest, mitigated by intentional movement, and maximum on sustained posture, the tremor was usually bilateral though not bilaterally synchronous. In coma the tremor disappeared but could occasionally be appreciated by gentle elevation or passive movement of a limb.

Less specific findings included increased tendon reflexes and muscle tone (usually of paratonic type) with ankle clonus and normal plantar responses. This unusual association was seen in 4 patients, while 7 others exhibited one or more of these signs. As coma deepened, muscle tone became flaccid, previously brisk clonus and tendon reflexes could no longer be elicited, and the plantar responses became extensor.

The diffuse nature of the cerebral disturbance was further shown by reversed sleep rhythm, excessive appetite, muscle twitchings, grasping and sucking reflexes, and disorders of speech and vision.

Case-reports

The patients have been classified according to whether the neurological changes were persistent, transient, or terminal.

PERSISTENT NEUROLOGICAL DISTURBANCE

These 5 patients exhibited constant though variable neurological abnormalities over periods ranging from eight months to more than three years.

Case 1.—Nonconformist minister, aged 59. Portal cirrhosis (ætiology unknown); occluded portal vein.

In July, 1952, tremor of the hands developed which was aggravated by excitement. During the next year this increased and there were episodes of somnolence, lasting up to four days. In these attacks he mumbled incoherently and failed to recognise close relatives; the tremor was exaggerated immediately afterwards.

Transient ascites and ankle œdema with hepatomegaly led to a diagnosis of cirrhosis of the liver, and he was treated with a diet containing 300 g. protein and 3 g. methionine daily. He became drowsy, disorientated, and incontinent with frequent lapses into coma.

In March, 1954, when first admitted to Hammersmith Hospital, he was found to have "flapping" tremor of the limbs, and tremor of the jaw, mouth, and tongue, with a vacant expression, frequent grimacing, and sialorrhœa. Consciousness was clouded by confusion, apathy, and sometimes coma, while his behaviour was frequently bizarre and inappropriate. Speech was slow, slurred, and impoverished.

Exacerbations followed a diet containing more than 70 g. protein or containing added methionine or ammonium chloride. On 20 g. protein daily he was virtually normal and he was discharged socially acceptable taking a 50 g. protein diet.

Case 2.—Housewife, aged 56. Cirrhosis (post-hepatitis); occluded portal vein.

In March, 1951, eighteen months after a severe attack of infective hepatitis, she suddenly became comatose for five days. On recovery she was confused, apathetic, and tremulous, and this persisted with frequent lapses into coma. Before attacks she is vacant in expression and dazed; on recovery speech is slow, slurred, and often irrational, her features are distorted by blinking and grimacing, and her actions are without reason. Throughout the whole period uniformly increased tendon reflexes, ankle clonus, and muscular rigidity have been elicited.

On admission to Hammersmith Hospital in March, 1954, these signs were found to vary with the intake of nitrogenous substances. On a diet containing 20 g. protein very little disorder was evident, but protein in excess of 60 g. produced marked deterioration. Exacerbations were provoked by methionine and ammonium chloride. She was discharged *greatly improved on a diet containing 50 g. protein.*

Case 3.—Welder, aged 42. Portal cirrhosis (ætiology unknown); portacaval anastomosis.

In January, 1952, an end-to-side portacaval anastomosis was constructed successfully following hæmatemesis from ruptured œsophageal varices. *He remained well though* lethargic till January, 1953, when he became mentally confused for a few hours. Frequent recurrences followed, usually at night, when he would wander about stumbling into walls and urinating on the floor. At other times he felt *overwhelmingly tired.*

In October, 1953, he developed a constant tremor of the hands and ataxia with muscle rigidity, ankle clonus, and exaggerated tendon reflexes. Mental confusion persisted.

In April, 1954, a low-protein diet (of 20 g. daily) produced *marked and sustained improvement while methionine (12 g.* daily) induced an exacerbation. Trans-splenic portal venography showed that the portacaval anastomosis remained patent, while serial liver-function tests suggest some deterioration in liver function since operation.

Case 4.—*Housewife, aged 36. Portal cirrhosis (ætiology* unknown); occluded portal vein.

Portal cirrhosis was diagnosed in 1943. Three years later she complained of feeling tired and tremulous. In 1948 ascites developed and she was noted to be apathetic, with tremor *of the hands, ataxic gait, and increased tendon reflexes.* In 1949 she was lethargic, forgetful, and somnolent, once being admitted incoherent and confused. She was treated as a case of psychomotor epilepsy and the association of the neurological disturbance with the liver disease was not recognised. Later in 1949 death resulted from severe hæmorrhage from an œsophageal varix. Necropsy revealed portal cirrhosis with thrombosis of the entire portal vein and an extensive portal collateral circulation.

Case 5.—Masseur, aged 51. Portal cirrhosis (ætiology unknown).

In May, 1949, this patient became recurrently somnolent, especially when hungry. Seven months later new symptoms appeared. *He was difficult to rouse in the morning, later* stumbling about, incoherent and behaving in an uninhibited and aggressive manner. Forgetful and lacking in insight, he became excessively loud and jocular, a caricature of his former personality. Variable coarse tremor of the hands with ataxia of gait developed and œdema and hepatosplenomegaly were noted.

In August, 1950, he died from acute pneumococcal meningitis. *At necropsy there was no naked-eye neurological* lesion to account for his earlier neurological symptoms. Cirrhosis of the liver with œsophageal varices was found, but there was no comment regarding the patency of the portal vein.

TRANSIENT NEUROLOGICAL DISTURBANCE

In this group of 7 patients neurological disorder was transient and did not exceed a week; complete recovery followed. Changes were often mild and could be assessed only by frequent neurological examination; the fully developed picture seen in the chronic group was observed in only one patient.

4 patients (9, 10, 11, and 12) had portal cirrhosis; 1 patient (8) had biliary cirrhosis; and 2 patients (6 and 7) were suffering from infective hepatitis.

Case 8.—Tailor, aged 60. Choledocholithiasis, cholangitis, biliary cirrhosis.

This patient had a six-year history of incomplete biliary obstruction with cholangitis. Sudden mental confusion and tremor was followed within two hours by severe melæna from a ruptured œsophageal varix. Two days later he was difficult to rouse and exhibited a gross tremor of the tongue and upper limbs, increased muscle tone in the legs, ankle clonus, and extensor plantar responses. Though variable, the neurological changes persisted for five days, terminating a day before the stools became normal in colour.

Case 10.—Housewife, aged 47. Portal cirrhosis (ætiology unknown).

After an initial period of sodium restriction augmented by ammonium chloride (2 g. t.d.s.) and a mercurial diuretic, 26 litres of ascitic fluid was removed slowly by paracentesis. The next day she was emotionally labile, alternately lacrimose and jovial, with a vacuous expression and "flapping" tremor of the hands. This disturbance lasted only one day.

TERMINAL NEUROLOGICAL DISTURBANCE

In this group of 6 patients the neurological changes usually developed in the course of severe hepatocellular failure and death ensued within eight days. The early onset of coma often modified the personality changes and motor disorder. 4 patients (13, 14, 15, 18) had portal cirrhosis which in 1 (18) was complicated by hepatoma. One patient (16) developed Chiari's syndrome secondary to renal carcinoma and another patient (17) died from serum hepatitis.

Case 14.—*Iraqi merchant, aged 50. Cirrhosis (alcoholic).* Uninfluenced by dietary sodium restriction and diuretics which included ammonium chloride 1 g. t.d.s., ascites accumulated and his general condition steadily deteriorated. Three weeks after beginning treatment he passed a melæna *stool and blood could be detected in the fæces until his death.* Two weeks later he became lethargic and doubly incontinent, with increased muscle tone and flapping tremor of the limbs. Deep coma supervened and this persisted till he died four days later.

Case 16.—Carpenter, aged 62. *Hypernephroma*; renal, inferior vena caval, and hepatic venous thromboses (Chiari's syndrome).

This patient became apathetic and confused with a flapping tremor of the upper limbs and brisk tendon reflexes. Hepatomegaly, ascites, gross ankle œdema, and prominent abdominal wall veins were observed. He rapidly became comatose and died six days later, the diagnosis being confirmed at autopsy.

Case 17.—Street trader, aged 48. Serum hepatitis of six weeks' duration.

Treatment, which included high-protein diet, had failed to affect the deterioration in this patient's condition, and after five weeks he developed ascites, becoming apathetic and later comatose. At this time tremor of the limbs and trunk could be appreciated, while muscle tone and tendon reflexes were increased in the upper limbs. Coma increased and he died four days after admission.

Electro-encephalographic Changes

The tracing was similar in 7 (cases 1, 2, 3, 4, 5, 9, 11) of 8 patients investigated. Bilaterally synchronous slow waves in the delta range, occasionally occurring *in bursts, were superimposed on a normal rhythm.* Such changes have been reported previously in patients in hepatic coma and pre-coma (Adams and Foley 1953).

Predisposing and Exciting Factors

Three important clinical factors became evident—portal-systemic venous collaterals, hepatocellular disease, and nitrogenous substances in the intestine. The relative influence of each varied in individual patients (see table).

The 5 patients with chronic symptoms suffered from portal cirrhosis, but in none was liver function severely impaired. In every case, however, extensive portal-systemic venous communications could be demonstrated. In 3, thrombosis of the portal vein deviated the whole portal blood-flow through collateral channels, and a 4th patient developed symptoms following end-to-side portacaval anastomosis. The 5th patient had œsophageal

varices, but detailed information regarding the extent of the collateral circulation is not available. A significant collateral circulation was also demonstrated in 6 other patients (8, 10, 13, 14, 15, 18).

Severe liver damage was more important in the transient and terminal groups. In 4 patients (6, 7, 16, 17) the changes were associated with extreme hepatocellular disease alone, while in 6 others there were the additional insults of hæmorrhage (8, 13, 14), surgical operation (15), paracentesis abdominis (10, 13, 18), and infection (12).

In 3 patients (1, 2, 9) the neurological signs were precipitated or enhanced by the administration of ammonium chloride (10 g. daily for four to six days), while smaller therapeutic doses of ammonium chloride (3–6 g. daily) may have had an adverse effect on 4 patients (7, 10, 13, 14) with severe liver disease. In 4 patients (1, 2, 3, 11) signs were markedly aggravated by increasing dietary protein above 60 g. daily and by giving methionine (10 g. daily for two or three days). Undue sensitivity to nitrogenous substances was particularly pronounced in the group with persistent signs. Gastro-intestinal bleeding not only depressed liver function but also increased nitrogen in the intestine.

Ammonia Metabolism

Portal venous blood contains a high level of ammonia, presumably derived from the nitrogenous contents of the intestine (Kirk 1936), which is metabolised as the blood passes through the liver. Elevation of the systemic blood ammonium level could arise from failure of the liver to metabolise ammonia reaching it from the portal blood or by diversion of portal venous blood into collateral channels. In all patients with neurological complications, the fasting level of ammonium in the peripheral blood was above the upper limit of normal (1 µg. NH_4N per ml.) and above mean levels found in patients with liver disease uncomplicated by nervous disorder (see table).

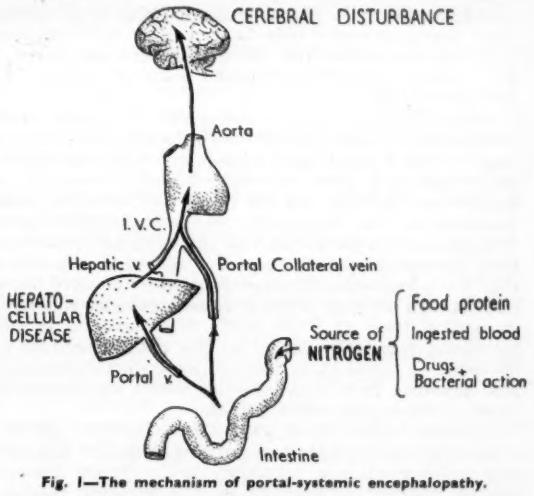

Fig. 1—The mechanism of portal-systemic encephalopathy.

In patients with severe hepatocellular damage the ammonium levels in the hepatic veins exceeded those in the peripheral veins, indicating that ammonium carried in the portal vein was passing through a damaged liver. Conversely, in patients with extensive portal-

PORTAL COLLATERAL CIRCULATION, HEPATOCELLULAR DISEASE, AND EXCITING AGENTS ARE COMPARED WITH AMMONIUM LEVELS IN PERIPHERAL AND HEPATIC VEINS

	—	Age and sex	Diagnosis	Portal venous collateral circulation	Hepato-cellular disease	Fasting blood-ammonium NH_4N µg. per ml.		Exciting agents						
						Peripheral vein	Hepatic vein	High-protein diet	Ammonium chloride	Methionine	Gastro-intestinal hæmorrhage	Paracentesis or operation	Infection	Extreme liver failure
CENTRAL NERVOUS SYSTEM SIGNS	PERSISTENT	1	M 59	*Portal cirrhosis*	+ + + (V) Thrombosed portal vein	+ +	1·55	1·20	×	×	×				
		2	F 56	,, ,,	+ + + (V) Thrombosed portal vein	+ +	1·41	0·71	×	×	×				
		3	M 42	,, ,,	+ + + (V) Patent porta-caval shunt	+ +	2·46		×	×	×				
		4	F 36	,, ,,	+ + + (A) Thrombosed portal vein	+ +						×			
		5	M 51	,, ,,	+ + (A)	+									
	TRANSIENT	6	F 29	*Infective hepatitis*		+ + +	1·96	2·57							×
		7	F 53	,, ,,		+ + +	1·03	1·33		×					×
		8	M 60	Biliary cirrhosis	+ + (V) (A)	+ +	1·99	1·60				×			
		9	M 19	Portal cirrhosis	O (B)	+ +	1·55			×					
		10	F 47	,, ,,	+ + + (A)	+ +	1·68			×			×		
		11	F 46	,, ,,	O (V)	+ + +	1·68		×		×				
		12	F 25	,, ,,	O (B)	+ + +	1·49							×	
	TERMINAL	13	F 52	,, ,,	+ + + (V) (A)	+ + +	2·22	1·75		×		×	×		×
		14	M 50	,, ,,	+ + (B)	+ + +	2·21	3·31		×		×			×
		15	F 65	,, ,,	+ + (A)	+ + +	1·50						×		
		16	M 62	Chiari's syndrome	! + (A)	+ + +	2·20								×
		17	M 48	Serum hepatitis	O (A)	+ + +	2·18	3·80							×
		18	M 52	Portal cirrhosis and hepatoma	+ (A) Thrombosed portal vein	+ +	2·58						×		
						0·78 (±0·12)	0·72 (±0·11)	← Normal values (7 patients)							
						0·92 (±0·16)	0·98 (±0·26)	← Liver disease without neurological disorder (17 patients)							

A = examined at necropsy or operation. B = barium swallow and meal. V = trans-splenic portal venography.
The extent of portal venous-collateral circulation and hepatocellular disease is graded as O, +, + +, or + + +.

systemic collaterals, the ammonium levels in peripheral veins usually exceeded those in the hepatic veins, suggesting that ammonium from the portal veins was entering the systemic circulation without passing through the liver (see table).

These findings were emphasised by giving oral ammonium chloride. In a patient with infective hepatitis (case 7) the fasting blood-ammonium level was raised, an exaggerated peak followed the administration of ammonium chloride, and the return to the initial value was delayed. The abnormality was greater in the hepatic vein than in the peripheral vein and confirmed extensive liver damage in the absence of a collateral circulation (fig. 2). Ammonia tolerance was also impaired in a patient with cirrhosis of the liver and extensive collateral circulation (case 1). The levels of ammonium in the peripheral veins were higher in this patient because of diversion of portal blood through anastomotic channels, but impaired liver function was shown by abnormal levels in the hepatic veins (fig. 3).

Detailed results await publication elsewhere (White et al. 1954), but in all 11 of the patients studied by hepatic-vein catheterisation a circulatory pathway was demonstrated whereby ammonium in the intestine reached the systemic circulation without being metabolised by the liver.

Other Investigations

Hyponatræmia was common in patients with ascites, and a terminal elevation of blood-urea levels was seen in fatal cases. In no patient was there significant acidosis or hypoglycæmia.

Apart from elevated ammonium levels, no biochemical or serological abnormality was detected in the cerebrospinal fluid in 7 of these patients.

Urinary copper was not excessive in patients 1, 2, and 9, thus excluding Wilson's disease (Bearn 1953).

Discussion

Despite the varied ætiology of the liver disease, the neurological picture suggested a common pattern, the disturbance differing in degree, duration, and extent. The signs change rapidly, are often reversible, and can be induced by nitrogenous substances—characteristics which favour a metabolic origin. Objective signs indicate

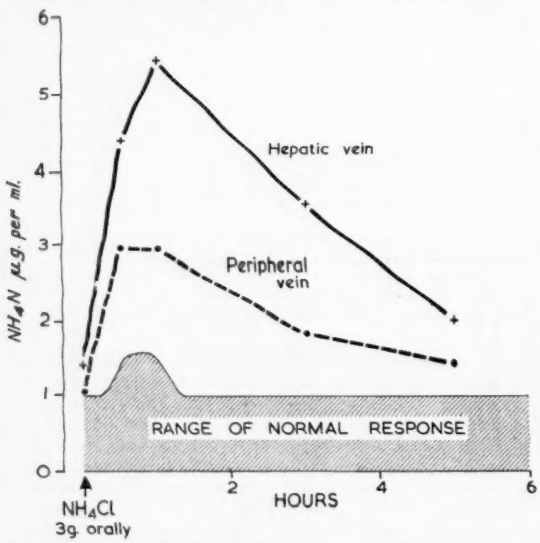

Fig. 2.—Simultaneous samples from peripheral and hepatic veins showing abnormal blood-ammonium curves following administration of 3 g. ammonium chloride by mouth in a patient with infective hepatitis.

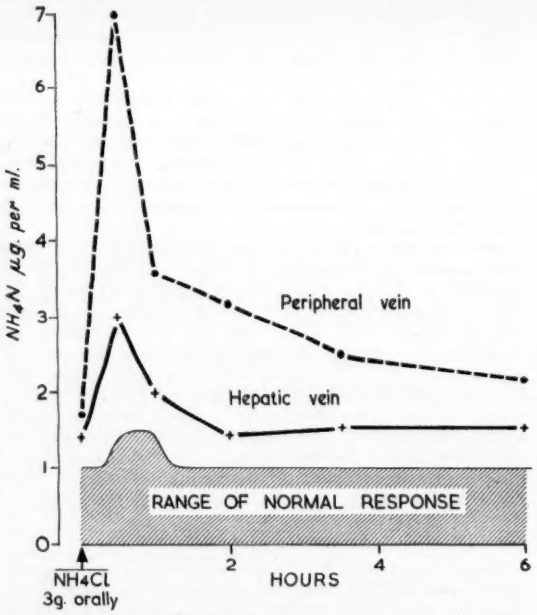

Fig. 3—Blood-ammonium curves following administration of 3 g. ammonium chloride by mouth in a patient with cirrhosis of the liver and extensive portal collateral circulation.

major involvement of the basal ganglia (which are particularly prone to toxic influences), the frontal cortex, and pyramidal systems; but critical appraisal suggests a diffuse cerebral disturbance.

Transient disorders of consciousness with elevated blood-ammonium levels have been reported in some cases of cirrhosis of the liver following large doses of ammonium salts by mouth (Van Caulaert et al. 1932, Kirk 1936). An altered mental state, characteristic tremor, and electro-encephalographic changes indistinguishable from impending hepatic coma, were produced in a proportion of patients by the administration of other nitrogenous substances from which ammonia could be derived (Phillips et al. 1952). We found elevated fasting blood-ammonium levels in our patients and were able to reproduce the neurological disturbance by the use of a high-protein diet and ammonium chloride. Identical changes followed methionine and we were impressed by its comparatively rapid effect. We also confirmed that the elevation of peripheral blood-ammonium could not always be correlated with the neurological state (Traeger et al. 1954). Daily estimations in individual patients reflected to some extent the degree of nervous disorder but critical levels showed great variation in different patients. At present the blood-ammonium is the only estimation which correlates at all closely with the neurological state, and the raised level of ammonium in the cerebrospinal fluid is further evidence of disturbed ammonium metabolism.

Kirk (1936) emphasised the importance of portal collateral vessels in ammonia intolerance in patients with cirrhosis, and Eck-fistula dogs which are given meat develop "encephalitis" (Balo and Korpassy 1932). Recently McDermott and Adams (1954) described a patient with a portacaval anastomosis who developed intermittent stupor which could be provoked by ammonium chloride. The sensitivity of our patients to nitrogenous substances could be directly related to the presence of an abnormal route through which portal venous blood entered the systemic circulation without being metabolised by the liver. The pathway lay through a damaged liver, through portal systemic collateral

channels, or through both. We believe that a nitrogen-containing substance in portal blood can thus cause a diffuse cerebral intoxication which we have termed portal-systemic encephalopathy (fig. 1).

In the absence of a portal collateral circulation only patients with very severe liver disease exhibited the syndrome, but exciting agents had no effect on 2 patients with thrombosed portal veins but good liver function, nor on another with severe liver disease without a collateral circulation. It is uncertain whether the syndrome can be due to an extensive portal-systemic collateral circulation in the absence of liver damage.

The neurological changes have often been attributed to hepatic failure, and certainly this is one method by which they can arise. In all the patients studied, a route existed whereby toxic nitrogenous substances carried in the portal vein might provoke cerebral disturbance; but this does not imply that every neurological disorder in patients with liver disease results from such intoxication. Adams and Foley (1953) used the term hepatic coma to embrace the entire syndrome of disturbed central-nervous function incident to liver disease. This term, however, may be misleading, for in many instances coma does not occur.

Disorders of consciousness and motor activity in patients with liver disease are not uncommon, and 16 of these patients were admitted to hospital during a six-month period.

The group in whom the neurological disturbance dominated the clinical picture over a long period is particularly interesting. Because of their antisocial behaviour and obscure physical signs, such patients may be investigated and treated as hopeless neurological or psychiatric problems. Portal-systemic encephalopathy should always be considered in patients with the characteristic disorder of consciousness and motor function, while occlusion of the portal vein should be suspected if the disorder persists. Identical signs, of varying severity, can follow portal-systemic anastomosis. The incidence of this complication is uncertain, but some postoperative deaths may be due to portal-systemic encephalopathy.

TREATMENT

If a specific exciting agent can be identified it should be withdrawn or treated. Caloric requirements should be supplied with glucose delivered by the simplest route, and nitrogen intake, whether in food or drugs, should be reduced to a minimum. Chemotherapy may be used to reduce bacterial action in the intestines, and the bowels should be emptied with an enema, a daily action being ensured subsequently by an effective purge. Minor episodes respond well to this régime, and the management of comatose patients in liver failure is similar. Glutamic acid or sodium glutamate, recommended by Walshe (1953), has been used on 10 occasions without apparent effect on the clinical condition or sustained fall of the blood-ammonium level. Others have shared this experience (Singh et al. 1954, Webster and Davidson 1954). Patients with persistent neurological disorder respond well when placed on the lowest protein intake compatible with mental and nitrogenous equilibrium.

High-protein diet, casein hydrolysates, amino-acid supplements, and ammonium chloride are widely used in liver disease. These measures are not contra-indicated, but their potential dangers must be recognised and anticipated.

Summary

The neurological complications observed in 18 patients with liver disease are described, and their relation to hepatocellular disease, portal collateral circulation, and exciting agents is demonstrated.

A syndrome associated with thrombotic occlusion of the portal vein in patients with cirrhosis of the liver, or arising as a sequel to portal-systemic shunt operations, is described.

Evidence is advanced that nitrogenous substances of portal venous origin, normally metabolised in the liver, may reach the systemic circulation through a damaged liver, through portal collateral channels, or through both, and cause a cerebral disturbance (portal-systemic encephalopathy).

The nature of the metabolic disorder is considered, with particular reference to deranged ammonia metabolism.

Principles of treatment are discussed.

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PATHWAYS OF INFLUENZA SPREAD

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THE World Health Organisation's programme for international study of influenza has included the collection of influenza virus strains from many countries. We have had an opportunity of testing most of these strains sent to us by collaborating W.H.O. influenza laboratories. During the past four years we have examined nearly 400 strains of influenza virus A, which could almost all be assigned to one of two distinct antigenic groups. The distribution of these strains in different countries and different years has not occurred at random but appears to have followed a definite sequence. The purpose of this report is to show the distribution of strains and to interpret, as far as possible, its significance in the understanding of influenzal epidemiology.

Basis for Antigenic Grouping of Strains

All the strains of virus were isolated and maintained by growth in fertile hens' eggs and were grouped antigenically from the results of agglutination-inhibition tests with ferret antisera (W.H.O. Expert Committee on Influenza 1953). Influenza virus A strains do not show the sharply distinct antigenic groupings found with many other viruses and bacteria, and ideally therefore strains should be compared by cross hæmagglutination-inhibition tests with homologous and hetero-

logous sera. It was impracticable to prepare antisera against all the strains we received, and sera were therefore prepared against representative strains. Cross hæmagglutination-inhibition tests with representative strains and their corresponding antisera revealed two distinct antigenic groups, which were called Liverpool (after A/England/1/51 virus, isolated from a severe outbreak of influenza in Liverpool 1950–51) and Scandinavian (of which A/Sweden/3/50 is a representative early strain, and A/Ned/1/53 a representative recent one). The validity of these antigenic groupings has been confirmed by tests with absorbed sera, which showed that Liverpool and Scandinavian viruses had distinct as well as shared antigens (Isaacs, Depoux, and Fiset 1954). The remaining strains were then examined by agglutination-inhibition tests with representative antisera of the two groups, and in most cases it was possible to assign a strain to one or other group. When the antigenic characters of a strain were still not clear, a ferret antiserum was prepared with this strain and tested against known strains of each group; usually the strain could now be grouped in this way. Antisera were not prepared against some strains, and there is still doubt about their antigenic grouping; they have been omitted from consideration at present. During the past four years strains of the Liverpool group have shown little antigenic variation and have been easily classified. Strains of the Scandinavian group have shown some antigenic variability, however, and considerable differences in their avidity for antibody (van der Veen and Mulder 1950). Elsewhere reasons have been put forward for considering them nevertheless as a single antigenic group. A few strains showing low avidity for antibody, and grouped earlier with the Scandinavian viruses on what we would now consider insufficient evidence, have been omitted from this report (in particular three South African and one Australian 1950 strains).

Results of Antigenic Grouping

Liverpool and Scandinavian strains received at the World Influenza Centre were arranged according to the country and year of isolation. The total numbers of strains of influenza virus A received varied considerably from year to year and from country to country. This variation was due in part to differences in the enthusiasm with which investigators isolated and transmitted strains of virus, but mainly to differences in the incidence of influenza from year to year. Thus major epidemics of influenza A in the northern hemisphere occurred in the 1950–51 and 1952–53 winters. Although the collection of strains is therefore not completely representative, it nevertheless shows some interesting features. In the accompanying table the strains received are arranged according to country and year of isolation and according to the predominant antigenic varieties found.

A total of 357 strains, comprising 103 Liverpool and 254 Scandinavian, were examined. Inspection of the table at once shows that these strains are not distributed at random. Most of the countries of northern and central Europe showed predominantly Scandinavian viruses. Liverpool viruses predominated in some countries of south-western Europe—Spain, Portugal, France, and Switzerland—and in some countries of south-eastern Europe and the Middle East—Greece, Turkey, and Israel. India and South Africa showed only Liverpool viruses. Where both types of virus were isolated in different years, the Scandinavian almost always took the place of Liverpool viruses, never the reverse.

Conclusions

(1) Both varieties of virus are capable of surviving up to four years in one country without significant antigenic variation, even though epidemics do not occur every year.

(2) In some countries Scandinavian viruses have taken the place of Liverpool viruses. The findings shown in the table could be interpreted as indicating that this substitution occurred before 1950 (if at all) in the countries of the first group, mainly in 1950–51 in those of the second group, in 1952–53 in Japan, U.S.A., and Canada, and in 1953–54 in Australia. We may guess further that this change will soon occur or be recognised in the countries of group IV, unless a new dominant antigenic variety of virus appears. The Liverpool strains are more closely related antigenically than are the Scandinavian to viruses prevalent in 1947 (formerly referred to as A-primes). This therefore appears to be another example of the supression of an earlier strain by a new antigenic variety. The finding is in keeping with the interesting observations of Davenport, Hennessy, and Francis (1953) that infection with influenza virus evokes antibody not only against the infecting strain but also against antigenic variants previously encountered. Such a situation would always favour the spread of new antigenic variants at the expense of older strains.

(3) Two strains of influenza A virus recovered during the past four years could not be grouped as either Liverpool or Scandinavian but appeared to be antigenically unique. One strain was isolated in Japan in the 1950–51 winter and the second from India in the 1953–54 winter. In both cases these unusual strains were antigenically very distant from all the other strains isolated at the same time, from other strains in our possession, and from each other. So far as can be judged at present, therefore, it appears that unique antigenic behaviour is not sufficient in itself for a strain to cause major influenza outbreaks.

(4) The simultaneous appearance in Japan, U.S.A., and Canada during the 1952–53 outbreak of Scandinavian

ORIGIN AND ANTIGENIC CHARACTER OF 357 STRAINS RECEIVED AT WORLD INFLUENZA CENTRE

	1950–51	1951–52	1952–53	1953–54
I. Countries showing only "Scandinavian" viruses:				
Sweden	13□		1□	4□
Denmark	6□		3□	1□
Belgium	1□		1□	
Germany	1□		7□	5□
Iceland	2□		2□	
Yugoslavia	1□		1□	
II. Countries showing predominantly "Scandinavian" viruses:				
Finland	1□		19□ 4●	1□
U.K.	8● 4□		1● 10 1□	8□*
Eire	1● 4□		1□	2□
Italy	1● 5□		17□	
Netherlands	1● 4□		7□	
III. Countries showing supersession of "Liverpool" by "Scandinavian" viruses:				
Japan	7●		2□	
U.S.A.	1●*		14□	3□
Canada	5●		1□	
Australia	1●	1●	2●	3□
IV. Countries showing only "Liverpool" viruses:				
South Africa	9●	8●		4●†
India	6●			3●
Turkey	3●	1●		
Portugal			19●	
Spain	2●			
Greece	1●			
Switzerland			2●	
V. Countries showing mixed types:				
France	1●		5● 4□	
Israel	3●		2□	1●
Malaya				1● 2□

□ "Scandinavian." ● "Liverpool."

* One Liverpool virus was recovered from a passenger who had just arrived in the United Kingdom in a ship from South Africa, where Liverpool viruses were prevalent.

* Other Liverpool viruses were reported by Dr. T. P. Magill.

† Four more Liverpool strains have recently arrived from South Africa.

viruses, which were antigenically indistinguishable from those recovered in Europe, is a further example of the rapid intercontinental spread of virus characteristic of influenza epidemics (Isaacs and Andrewes 1951).

(5) It has been of particular interest to note the presence of Scandinavian virus in a large area of north-west Europe over a period of four years, and a similar situation with Liverpool virus in South Africa and India. These findings favour the hypothesis that virus has survived locally during this time rather than that virus has died out in inter-epidemic periods and been reintroduced later. There is more than a suggestion from these results that the presence of one virus type in an area tends to exclude the other type, a finding which is difficult to interpret unless we assume virus to be quite widely seeded in an area during an inter-epidemic period. From such an area virus would spread outwards during epidemics to countries with susceptible populations.

(6) The immunity of populations of whole countries in Europe may be remarkably uniform from the epidemiological point of view. Such a hypothesis would help to explain (*a*) the presence of a single antigenic variety of virus over a large area; (*b*) the absence of outbreaks in many inter-epidemic years (e.g., 1951–52) when circumstantial evidence indicated that virus was present locally; and (c) the complete supersession of Liverpool by Scandinavian virus in some areas, though, as independent evidence suggests, it can clearly survive much longer in another population.

Summary

The distribution of two antigenic varieties of influenza virus A among some 400 strains received at the World Influenza Centre during the past four years has been studied.

The two antigenic varieties were not distributed at random, but their appearance seems to have followed a definite sequence in different countries.

To explain the distributions of virus found and the supersession of one virus variant by another, it is suggested that the immunity of a large proportion of the population in different countries may be remarkably uniform from the epidemiological point of view

We should like to thank Dr. C. H. Andrewes, F.R.S., for his most valuable advice and criticism. We should also like to thank our colleagues in W.H.O. laboratories in many countries who sent us virus strains; and Dr. T. P. Magill, of the Strain Study Centre, New York, for his coöperation and helpful discussions.

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"... Although only one old person specifically said she was very anxious to have a visitor, the fact that many often want more company than they have is apparent, not only in the pleasure which the field worker's calls gave but in such remarks as 'not even the vicar calls now.' The lack of parochial visiting was felt and remarked upon by several. It was clear, however, that discretion in visiting is needed. Confidence has to be won, particularly amongst those who have 'never asked anything of anyone.' The brief case or papers in the hand suggest a welfare worker, which is not welcomed. The plain envelope for correspondence is necessary to avoid fear of gossip. The wrong knock obtains no reply. The unannounced arrival causes a flutter. Acceptance of the role of the lady doctor calling may be necessary. Willingness to view false legs is as important as willingness to chat. 'Good day' and not 'good-bye' must be said, as the second suggests death before the next meeting."
—From *Over Seventy*, a report of the National Old People's Welfare Committee. London, 1954; p. 34.

HOSPITAL GASTRO-ENTERITIS

AN EPIDEMIOLOGICAL SURVEY OF INFANTILE DIARRHŒA AND VOMITING CONTRACTED IN A CHILDREN'S HOSPITAL

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THIS survey is concerned primarily with cases admitted to the infants' ward of a children's hospital *for conditions other than gastro-enteritis* in the six years September, 1947, to August, 1953. Before September, 1947, admissions to the infants' ward included cases of primary infantile diarrhœa and vomiting; but from that time onwards such cases have been admitted to a separate unit in another part of the hospital. Nevertheless infantile diarrhœa and vomiting acquired in hospital ("hospital gastro-enteritis") have continued to smoulder in the infants' ward and at times reached epidemic proportions.

We report here our personal observations—clinical and bacteriological—on some outbreaks of hospital gastro-enteritis against the wider background of its changing incidence and mortality in those six years. We also describe what appears to be an adequate preventive routine for the infants' ward and discuss the repercussions of this routine on the gastro-enteritis unit. We do not claim to have discovered anything new in the ætiology of the condition, but we bring forward evidence in substantiation of previously published ideas which have not been universally accepted (Holzel et al. 1949, Payne and Cook 1950, Cathie and MacFarlane 1951, Shanks and Studzinski 1952, Scott 1953, Wolfish 1953, Lowdon 1954).

The Ward

The infants' ward is one of three in the main block of a children's hospital dating from 1881. It is a large open ward measuring 58 ft. by 22 ft. Along its south side, but separate from the ward, is a glass-protected balcony accommodating cots for toddlers, with a small enclosed section at one end used in recent years for septic cases. At the west end of the body of the ward there is another separate annexe, in which are nursed infants up to the age of 3 months believed to be free from infection. Newborn babies and, especially, premature infants are admitted to the latter section. In both annexes there are glass partitions 6 ft. high between the cots, but on the rest of the balcony and in the ward itself there are no artificial divisions.

The capacity of the infants' ward has varied. During the first four years of the period under review it accommodated 28 cots, but during the last two years we have worked with a maximum of 20 cots, which we have found to be a satisfactory compromise between the requirements of an active unit and the need to keep cross-infection to a minimum. The ward accepts infants of any age from a few hours to 2 years, including sickly premature infants; and the smaller infants are very vulnerable. Infections, especially gastro-enteritis, prevent the ward from performing its essential function.

Sources of Information

For descriptive purposes it is convenient to subdivide the survey broadly into three periods as follows:

Period I: September, 1947, to March 27, 1950 (thirty-one months). None of the infants surveyed was known to us, and no special bacteriological investigation of gastro-enteritis was made; but the morbidity and mortality were determined.

Period II: March 28, 1950, to August, 1951 (seventeen months). Only during the last five months of this period were

cases under the clinical supervision of one or more of us. However, from March 28, 1950, onwards the facilities afforded by the Public Health Laboratory were used for diagnosis, and throughout this stage they were gradually extended for the epidemiological control of gastro-enteritis.

Period III: September, 1951, to August, 1953 (twenty-four months). All the infants surveyed were under the personal observation of one or more of us, and the facilities available from the Public Health Laboratory were more extensively used.

From April, 1951, onwards detailed clinical data are available. Cases of hospital gastro-enteritis before this were traced through the ward admission book, which gives the diagnoses of all babies passing through the ward. All medical records of infants with one or other of the following diagnoses were carefully scrutinised: diarrhœa and/or vomiting, dietetic upset, feeding problem, and gastro-enteritis. Cases were excluded in which an element of doubt existed about the diagnosis of "hospital gastro-enteritis," or where bowel symptoms appeared during the first three days in hospital. This method of selection is likely to have yielded a conservative estimate of morbidity. Bacteriological reports on individual cases were not included in the notes and did not therefore bias the clinical abstractors during their assessment.

The medical records of all infants dying in the ward before April, 1951, were carefully reviewed. As the clinical picture of severe and fatal gastro-enteritis is generally clear-cut, we believe our figures give an accurate picture of the mortality from hospital gastro-enteritis. Negative necropsy findings provided additional evidence for the inclusion of many of the cases.

Bacteriological Methods

The specimens submitted for examination were stools and rectal swabs, care being taken that the swabs were inserted into the rectum and soiled with fæces. All the stools and rectal swabs were plated out on MacConkey's medium and, in cases with gastro-enteritis, on media for the isolation of shigellæ and salmonellæ. After overnight incubation at 37°C the plates were examined under a wide-field binocular plate microscope, and the number of colonial types of lactose fermenters was determined. Representatives of every lactose-fermenting colonial type were picked, at least six colonies being selected from each plate. (This rule was relaxed when all the colonies present were of the same colonial type which differed unequivocally from *Escherichia coli*, as occasionally obtained when apparently pure cultures of *Bacterium ærogenes* were encountered.)

Colony picks were tested by slide agglutination with a pooled serum made by mixing suitable dilutions of high-titre *Esch. coli* O group 111: B,4 and O group 55: B,5 sera in such proportions that the K titre by tube agglutination of each individual component lay between 1/100 and 1/200. The individual high-titre sera were kindly supplied initially by Dr. Joan Taylor and later by the Standards Laboratory.

Colonies which gave a homogeneous suspension in physiological saline solution and were agglutinated by the pooled serum were then tested by slide agglutination against the individual components of the pooled serum to verify that agglutination had been due to the presence of antigen B,4 or B,5. The remainder of the colony was subcultured on a tryptic digest agar slope and incubated at 37°C. After five to twenty-four hours' incubation at 37°C the slope was washed off with sterile physiological saline solution, and part of the ensuing suspension was steamed for two hours. After dilution to standard opacity the latter was put up in a range of four or five doubling dilutions together with a control, by tube agglutination in a water-bath at 50°C against the homologous serum of appropriate known O titre (dilutions often used were 1/2, 1/4, 1/8, 1/16, and 1/32 of a serum with a titre of about 1/16.) On rare occasions when the steamed suspension agglutinated spontaneously in physiological saline solution the unheated portion of the suspension was diluted to standard opacity and put up in a similar manner by tube agglutination at 37°C with the homologous serum of appropriate K titre.

No case or excreter of *Esch. coli* O group 111: B,4 or of O group 55: B,5 was reported until the organism isolated had been agglutinated to titre either with the appropriate O or with the appropriate K serum, but only in relatively few instances was confirmation by tube agglutination *both* of the O and of the K antigen looked for and obtained.

For the sake of brevity we shall hereafter refer in this report to organisms which satisfied these criteria as "O,55" and "O,111" respectively, and collectively to them as specific types of *Esch. coli*. We shall also refer to the gastro-enteritis which we believe they evoke as "coliform diarrhœa."*

Clinical Survey

PERIOD I: September, 1947, to March 27, 1950

For obvious reasons it is not within the scope of this survey to enlarge on period I. Hospital gastro-enteritis was endemic in the infants' ward throughout the period and assumed epidemic proportions during February and March, 1950, when there were 13 cases, 10 of which were fatal (fig. 1).

PERIOD II: March 28, 1950, to August, 1951

This period provided a wealth of clinical and epidemiological information. Laboratory examinations, which began on March 28, soon showed that the outbreak, which had started during the latter end of period I, was largely (if not wholly) due to O,111, this organism being isolated from every one of 10 clinical cases tested (fig. 2). The outbreak was short-lived, and during the latter half of April only 1 other baby contracting hospital gastro-enteritis was found to be infected with O,111. Eight months later a further isolated example of O,111 infection was found in a child aged 6 weeks who developed diarrhœa in December, 1950. She was treated with chloramphenicol from the moment that suggestive symptoms were exhibited, and did not transmit her infection to others in the ward.

In the middle of April, 1950, there occurred in the infants' ward an incident which was to make its repercussion felt in the hospital for eighteen months. A boy, aged 8 months, was admitted to the ward from a convalescent home for infants. By next morning it had become clear that he had gastro-enteritis, and he was transferred to the gastro-enteritis unit, a stool being sent for laboratory examination. This stool contained O,55. From this 1 case, which was in the infants' ward for only one day, direct case-to-case cross-infection can be traced within the ward until June of the following year—fifteen months. By this time O,55 had been transmitted serially to 127 children. If we can assume that this organism could and did on two occasions survive in fomites for forty-eight hours, a reasonable assumption in view of Rogers's (1951b) findings, this chain of case-to-case infection in the infants' ward can be followed still further until August, 1951 (seventeen months), when the ward was finally closed and emptied. By this time the number of cross-infections had risen to 137, of which about half (69) had been symptomless. This long outbreak due to O,55 (which we subsequently call the 1950–51 outbreak) just overlapped the earlier and more explosive outbreak due to O,111, and it follows that no break in the incidence of hospital gastro-enteritis in the infants' ward is apparent during the second period in fig. 1.

By the end of period II it was apparent that drastic action was necessary to break the chain of cross-infection in the infants' ward. A preliminary survey at this time revealed that in the previous year there had been 47 cases of hospital gastro-enteritis, and that 9 of these infants had died. The stools in 45 of the 47 cases had contained O,55 at the time of the bowel upset, and from 1 of the remaining cases O,111 had been isolated (fig. 2).

* Our more recent experiences have led us to add O group 26 B,6 and O group 128 B,12 sera to our routine test. We are also alerted to identify an outbreak of hospital gastro-enteritis due to any recognised specific type of *Esch. coli* other than those for which we test as a routine, through the courtesy of Dr. Joan Taylor's collaboration.

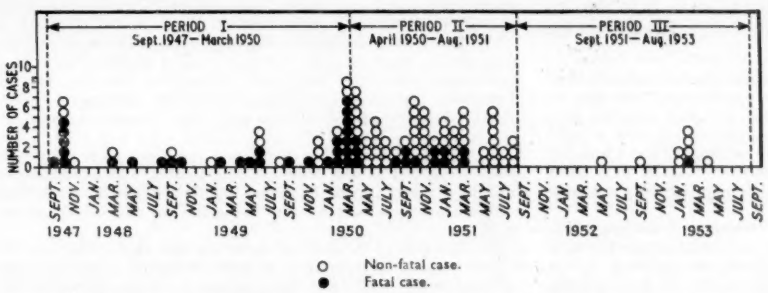

Fig. 1—Morbidity and mortality of gastro-enteritis acquired in infants' ward between September, 1947, and August, 1953.

The ward was accordingly closed to admissions at this point and rapidly cleared of all patients. Fumigation was carried out with formalin and a microsol spray, and for a month no new patients were admitted. A more drastic routine of preventive measures was introduced in the infants' ward as follows:

(1) The number of beds was reduced from 28 to 20.

(2) Admissions to the infants' ward were more carefully screened. Infants thought to have diarrhœa secondary to parenteral infection were admitted directly to the gastro-enteritis unit.

(3) The disposition of cases in the infants' ward was strictly supervised; the doctor admitting the infant allotted it to a particular cot; and no infant was moved to another position in the ward without the doctor's consent.

(4) Fæcal swabs were taken from all infants on admission and thereafter once a week during their stay in hospital. If either O,111 or O,55 was isolated, the ward was closed temporarily and the positive case excluded, whether symptoms were present or not. Daily swabs in all the remaining cases were then taken for three successive days, and if all were negative the ward was reopened. If there were further positive swabs, the ward was emptied as soon as possible and fumigated efficiently before being used afresh.

(5) If an infant developed sporadic diarrhœa and vomiting in the infants' ward, it was swabbed and transferred immediately to the gastro-enteritis unit without awaiting the laboratory findings.

(6) Bottle-feeds were pasteurised.

(7) Barrier nursing was done with greater thoroughness, including the immersion of napkins in "white fluid" (Medical Research Council 1951) at the bedside, and the application of spindle oil to the wooden floor.

Comment on the 1950–51 Outbreak

Through an inadequacy in the screening of admissions infection was introduced into the ward by a case of diarrhœa and vomiting. It was subsequently shown that this infant was excreting O,55 on admission.

During this long outbreak several unsuccessful attempts were made to rid the ward of infection; the ward was closed, partially emptied, and fumigated. We believe that the failure of these attempts was due to the insufficiently strict attention paid to those symptomless excreters for whom alternative accommodation could not be found; they were allowed to remain in the ward and maintained unbroken the chain of cross-infection.

Throughout the whole of period II the submission of specimens to the laboratory was somewhat capricious, though specimens were sent sooner or later from all the infants who developed symptoms of gastro-enteritis, except 1 who developed typical symptoms in June, 1951, shortly after being discharged home. Routine swabbing of admissions was not always enforced. For reasons which are not clear the laboratory was relatively little used during April, 1951, in which month only 10 specimens were sent for laboratory examination from the infants' ward, although the ward remained full and admitted 20 infants during the month. This accounts largely for the apparent gap in the chain of cross-infection shown in fig. 2, and we know that a child infected during March remained in the ward and continued excreting O,55 until half-way through May. If routine weekly swabs had been taken throughout period II, there can be little doubt that the number of infants found to be excreting O,55 would have been even greater than we have shown. Had systematic swabbing, however, been coupled with the immediate removal of all infected children, this outbreak might have followed a very different course, but it is only fair to point out that during this period experience was being acquired of coliform diarrhœa.

PERIOD III

September, 1951, to August, 1953

When the ward was reopened under the modified procedure, for sixteen months there were no further

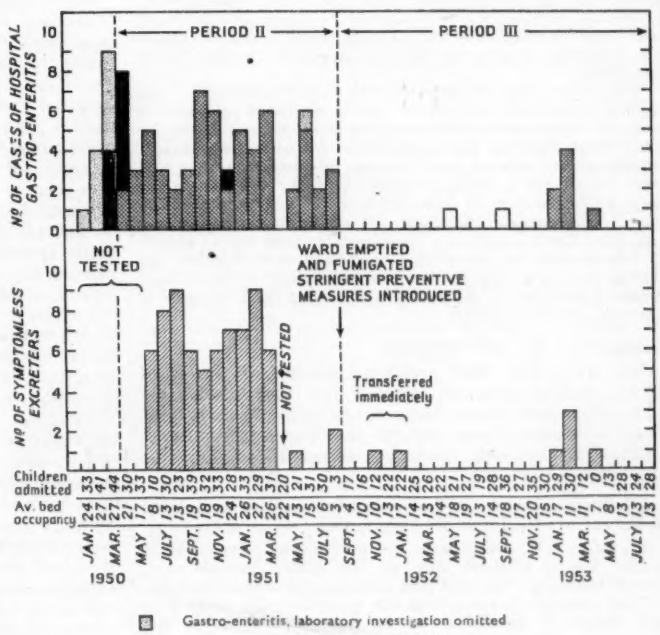

Fig. 2—Incidence of gastro-enteritis and infection with specific types of *Esch. coli.* in infants' ward during periods II and III. Infections unaccompanied by gastro-enteritis are shown in lower register.

cases of gastro-enteritis due to O,111 or to O,55 (fig. 2). In January, 1953, however, a small outbreak began which ran the following course :

On Jan. 19, A.B., a boy, aged 19 months, was admitted to the infants' ward with mild tracheobronchitis. There was no immediate history of gastro-enteritis, but five months previously he had been in the gastro-enteritis unit with a mild intestinal upset. On that occasion no pathogens were isolated from his rectal swab, though he was in contact with a child excreting O,55 and with several others who had only recently ceased to do so.

On his admission to the infants' ward in January, 1953, a fæcal swab was negative. From a routine swab taken a week later, however, on Jan. 25 O,55 was isolated. This positive result was received on Jan. 28, the child having been discharged home on the previous day. As he had had no diarrhœa or vomiting while in the ward, and as there were no other suspicious cases in the ward and no other positive swabs, it was decided slightly to relax our preventive routine by allowing the ward to remain open on a day-to-day basis under close clinical and bacteriological scrutiny. A fæcal swab from each patient was taken daily, and within three days of the receipt of notice of the first positive swab from A.B., another positive swab was reported, from a child in an adjacent cot.

The ward was closed to admissions and subsequently emptied and fumigated. Unfortunately, during these three days 6 new patients were admitted, 2 of whom later developed severe hospital gastro-enteritis. Altogether there were 8 cases in which the swab subsequently grew O,55, and 6 of these infants developed gastro-enteritis, 5 severe enough to require intravenous infusion (but this measure was withheld from a baby with severe hydrocephalus who died). The 2 symptomless excreters were twins aged 2 months and each weighing less than $4^1/_2$ lb. when they became infected.

When the ward was emptied, 1 of these babies was sent home, but the smaller one was moved to a room on the same floor some distance from the ward. This was done because it was considered imprudent to transfer such a small infant to the gastro-enteritis unit. The baby remained in the room for eleven days and was then discharged home. Concurrently a child aged 8 months in the newly reopened infants' ward was found to be infected with O,55 in a swab taken just before his discharge home; he did not, however, develop bowel symptoms.

We believe that his infection was acquired from the twin nursed outside the ward. This view is supported by a similar train of events when the same twin was readmitted to the same room nineteen days later. On this second occasion 2 infants in the infants' ward became infected with O,55 and were transferred to the gastro-enteritis unit. Once again the only known source of infection was the child outside the ward, who was still excreting the organism but remaining free from bowel symptoms. Fortunately there was no spread of infection to the rest of the ward from these 3 cases, nor during the remaining five months of the survey were there detected any further excreters of O,111 or O,55 or cases of hospital gastro-enteritis.†

Comment on the 1953 Outbreak

We have seen that prolonged closing of the ward at the end of period II, coupled with the introduction of rigorous preventive measures, was followed by sixteen months' freedom from coliform diarrhœa in the infants' ward. The outbreak which then followed brought home the following points :

(1) Strict adherence to the preventive measures formulated at the end of period II would have spared 2 severe cases.

(2) Case A.B. may have become infected five months earlier during a short stay in the gastro-enteritis unit. The outbreak he initiated demonstrates the serious problem of the symptomless intermittent excreter and underlines the danger of admitting to an infants' ward a patient who has previously been nursed in a gastro-enteritis unit. Even preliminary isolation pending the finding of three negative fæcal swabs might not have demonstrated this child's potential infectivity. Thus in early February, 1953, shortly after his discharge from hospital, six negative fæcal swabs were obtained on consecutive days. Nevertheless on an isolated follow-up visit at the end of February there was another positive swab (type O,55).

(3) The first 3 infants to develop symptoms were in cots adjacent to that occupied by A.B. All 3 children were in a debilitated state and had been in hospital for months, the diagnoses being hydrocephalus following meningitis, idiopathic hypercalcæmia of infancy, and emaciation due to rumination.

(4) All 6 infants who developed coliform gastro-enteritis were being fed at the time on cow's milk. Two premature infants (twins), aged 6 weeks, who became infected but remained symptom-free, were being fed on expressed breast-milk.

(5) The use of a near-by room on the same floor as the infants' ward for nursing a premature infant symptomlessly infected with O,55 was the apparent cause of reinfection of the ward after closure and fumigation.

Repercussion on Gastro-enteritis Unit of Preventive Measures Applied to Infants' Ward

During period III the gastro-enteritis unit, which consists of two open wards with no facilities for isolation, received four types of case :

(1) Primary gastro-enteritis.

(2) Diarrhœa and vomiting apparently secondary to parenteral infection—" secondary diarrhœa."

(3) Gastro-enteritis acquired in and transferred from (*a*) the infants' ward, (*b*) other hospitals, and (*c*) residential nurseries.

(4) Babies unfit for discharge from hospital and found by routine swabbing in the infants' ward to be excreting a specific type of *Esch. coli*, though without symptoms of gastro-enteritis.

The diversion to the gastro-enteritis unit of infants who on admission appear to have secondary diarrhœa undoubtedly exposes them to the risk of coliform diarrhœa when the causal organism is present in the ward. In the absence of facilities for isolation, however, we see no better alternative to this arrangement. The clinical appraisement of a case of diarrhœa and vomiting is often difficult, especially at first sight. The infant whose diarrhœa is attributed in the admitting-room to a parenteral focus of infection may be proved, once in the ward, to have been harbouring a pathogen in its stools from the time of admission. For example, 3 infants referred with obvious infections (pneumonia, otitis media, and pyelonephritis) accompanied by diarrhœa were proved later to be infected with O,55 on arrival at hospital. Fortunately, exclusion of this type of case from the infants' ward was the practice when these 3 infants with double infections presented.

The admission from time to time of children infected with specific serological types of *Esch. coli* seriously affects the smooth running of the gastro-enteritis unit, where, in spite of a continual influx of children with diarrhœa from their own homes, weeks may pass without the detection of a pathogen in the unit. During period II, when infants infected with O,55 were continually being admitted, the unit was seldom, if ever, free from coliform diarrhœa, many infants acquiring it by cross-infection within the unit. Similarly, the transfer of cases and excreters of O,55 during the 1953 outbreak had the same effect, and coliform diarrhœa smouldered on there for several months. Like Rogers (1951a), we have found that even the most careful barrier nursing often did not prevent the spread of specific types of *Esch. coli* to other infants in the ward from whom no known pathogens had previously been isolated. Such cross-infection, though occasionally symptomless, was often associated with a sudden violent relapse of diarrhœa and/or vomiting, coinciding in a dramatic way with the discovery of the organism in the stools for the first time. In some cases this relapse occurred a few days after a child had been discharged, apparently well, from the unit. On the other hand, when the unit was clear of known pathogens, particularly O,55, relapses and recurrences of diarrhœa and/or vomiting still occurred from time to time, but they seemed to lack the dramatic character of those associated

† There have been no further cases of hospital gastro-enteritis in in the nine months following the end of the survey period.

INCIDENCE OF O,55 INFECTION AND OF GASTRO-ENTERITIS IN CHILDREN SWABBED WITHIN 48 HOURS OF ADMISSION TO INFANTS' WARD

Children swabbed on admission	Period II (March 28, 1950–August, 1951)		Period III (September 1951–August, 1953)	
	Age-group (mos.)			
	0–12	More than 12	0–12	More than 12
Total number	174	73	427	118
No. acquiring hospital gastro-enteritis	44	1	9	0
No. admitted with gastro-enteritis	2	0	1	0
No. O,55-positive on admission ‡:				
(*a*) With symptoms of gastro-enteritis	2	0	1	0
(*b*) Without symptoms of gastro-enteritis	4	0	0	0
No. O,55-positive after admission *	97	11	13	2
No. with gastro-enteritis concurrently O,55-positive	45	1	8	0
Percentage O,55-positive on admission	3·4	0·0	0·2	0·0
*Percentage O,55-positive after admission**	*56*	*15*	*3·0*	*1·7*
Percentage O,55-positive among children with gastro-enteritis	*98*	*1/1*	*80*	*0/0*
Percentage O,55-positive among children without gastro-enteritis	41	14	1·2	1·7
Percentage acquiring hospital gastro-enteritis	*25*	*1·4*	*2·1*	*0·0*

* Includes children O,55-positive on admission.

with this organism. The intake to the gastro-enteritis unit of cases of hospital gastro-enteritis and excreters of specific types of *Esch. coli* from the infants' ward undoubtedly threw an added burden on the unit. However, since more drastic preventive measures were introduced in the infants' ward at the end of period II, there has been a sharp decline in morbidity from coliform diarrhœa in the hospital as a whole.

Epidemiology

During the early part of period II the laboratory was used only to throw light on suspected cases of gastro-enteritis, and routine swabbing on admission had not yet been introduced; moreover, during period II, after routine swabbing had been introduced it was not always done within forty-eight hours of admission (during period III it was the invariable rule to swab on the day of admission).

To supplement the incomplete bacteriological information thus obtained, a population was chosen for survey defined as children admitted to the infants' ward and swabbed within forty-eight hours. As this selected population is not identical with that reviewed in the clinical survey, the figures which follow do not necessarily correspond to those given in the rest of the report. As all except 1 of the cases of hospital gastro-enteritis ascribed to O,111 occurred early in period II before routine swabbing had been initiated (several had been infected in period I), this organism is seldom met with in our selected population.

The population surveyed during periods II and III has been subdivided by age into two groups: those aged 12 months or less, and those aged more than 12 months. In the accompanying table figures are given separately for each age-group. It is clearly shown that it was upon the lower age-group that the brunt of the clinical infections fell (53 out of 54 cases). The higher age-group did, however, play an important rôle as an added reservoir of symptomless infection during period II, and it was a member of this group who introduced O,55 into the ward and initiated the 1953 outbreak.

Two striking facts revealed in the table by the lower age-group during period II are as follows:

(1) A fourth of this group acquired gastro-enteritis while in hospital.

(2) The proportion of infants infected with O,55 rose from 3·4 to 56% during residence in the ward.‡

There can be no doubt that the conditions prevalent in the infants' ward at that time—namely, the proximity in an open ward of a group of artificially fed infants of whom one or more harboured specific types of *Esch. coli* (in this instance O,55)—were highly conducive to the dissemination of the organism. As similar conditions prevail in many institutions caring for very young infants, we believe that the lessons to be drawn here are of wide application.

As epidemiological data regarding the survey population are fairly extensive, they are reviewed to establish the clinical incubation period of our cases of diarrhœa due to O,55. We cannot rule out the possibility that incubation periods in a few of our cases may have fallen outside these limits, but every case in our series was consistent with an incubation period of four to eleven days. This finding is in agreement with that of the Aberdeen group (Giles et al. 1949, Smith et al. 1950).

We have referred to conditions conducive to the spread of coliform diarrhœa which may obtain in institutions catering for very young infants. To try to assess the part which convalescent homes, nurseries, and hospitals may have played in the local dissemination of coliform diarrhœa we have inquired into the movements of all O,55 positive-on-admission infants before they entered the children's hospital during periods II and III. 31 such infants were admitted, and it is significant that 19 of them yielded histories of recent residence in a hospital, nursery, or convalescent home.§

No history of direct institutional contact was obtained in 12 of these infants (whom we shall call "non-institutional" admissions), but they might still possibly have acquired their infections from institutional cases by less direct means. We have therefore plotted these non-institutional positive admissions (shown in fig. 3 in black)

‡ The proportion of infants infected with O,55 while in hospital may have been even higher than indicated. All the infants yielding O,55 in a first swab taken within forty-eight hours of admission have here been shown as positive on admission, but possibly some of these might have been examples of early swab-conversion after admission to hospital.

§ In a control series of 31 infants admitted during period II a history of recent institutional residence was obtained in 2 cases.

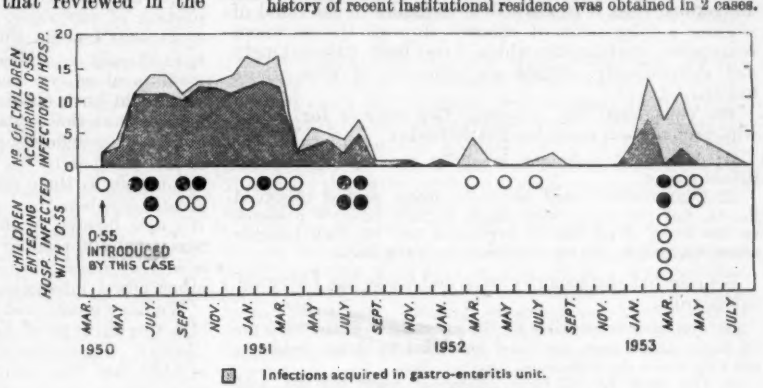
No. OF CHILDREN ACQUIRING O·55 INFECTION IN HOSP.
CHILDREN ENTERING HOSP. INFECTED WITH O·55
0·55 INTRODUCED BY THIS CASE
MAR. MAY JULY SEPT. NOV. JAN. MAR. MAY JULY SEPT. NOV. JAN. MAR. MAY JULY SEPT. NOV. JAN. MAR. MAY JULY
1950 1951 1952 1953
Infections acquired in gastro-enteritis unit.
" " " infants' ward.
Institutional positive admissions.
Non-institutional positive admissions.

Fig. 3—Time relationship of O,55-positive admissions to children's hospital with O,55 infection within hospital.

against the concurrent incidences of O,55 infections within the children's hospital. The close relationship shown, particularly the time-lag, provides evidence suggesting that the children's hospital also played a part in the dissemination of O,55 infection to the surrounding infant population as well as the other institutions to which we have made reference.

Also shown in fig. 3 are the O,55-positive "institutional" admissions. Since infections in other institutions need not necessarily bear a chronological relationship with those in the children's hospital, we did not expect these admissions necessarily to display a relationship with the peaks of O,55 infection in the children's hospital. In fact, however, this relationship also is fairly convincingly shown in the figure. It therefore seems that during this period there was a linkage of O,55 infection in the children's hospital with similar infection in neighbouring institutions caring for young children. In the light of our experiences such linkage is not difficult to imagine.

We have drawn attention to what we believe is a likely explanation for the observed time-distribution of O,55-positive admissions to the children's hospital. An alternative explanation might be that, since initial swabbing was done in the infants' ward itself, positive swab results thus obtained might have been due to very early cross-infections within the precincts of the ward. Though we cannot rule out this possibility in a few cases, this explanation is unlikely to be valid to the series as a whole, since it would be difficult on that basis to explain why "early cross-infections" should have had so great a predilection for infants admitted from other institutions.

A further point thrown into relief by fig. 3 is that each of the outbreaks of O,55 infection began in the infants' ward and was followed by a prolonged secondary wave of infection in the gastro-enteritis unit.

Discussion

Among the procedures which drastically curtailed the incidence of gastro-enteritis in the infants' ward during period III was one involving the heat treatment of assembled bottle-feeds. At an earlier date the nurses—who are trained to wash their hands with scrupulous care before handling feeds at the cot-side—were warned that on a certain morning tests would be made in an attempt to demonstrate the inadequacy, as a sterilising procedure, of their hand-washing technique. In spite of this warning, from the washed fingers and thumb of one of the nurses who an hour previously had made up the bed of an infant excreting O,55 this organism was easily recovered.

This episode emphasises a lesson which cannot too often be repeated—i.e., that hand-washing is potentially dangerous when it is allowed to engender in the mind of a nurse a false sense of security through the mistaken conception that hands which have been painstakingly and methodically washed are synonymous with sterile hands.

We considered the following two courses for nurses who prepare and assemble bottle-feeds:

(1) A surgical technique involving the use of sterilised rubber gloves.

(2) Conventional ward technique using washed ungloved hands, full provision being made for the possible presence on the latter of pathogenic organisms and for their possible entry, and subsequent multiplication, in the feeds.

We selected the second course and made the following safeguards:

(*a*) The nurse responsible for the preparation of the feeds for 24 hours ahead does not enter the ward until her duties in the milk room are completed for that day.

(*b*) The feeds having been assembled ready for use, and paper covers having been applied over the teats, are autoclaved for 5 minutes at 10 lb. pressure. We have found by experience that this raises the temperature of the feeds to 180°–190°F but does not caramelise the milk. The temperature of one feed is checked each time on removal.

(*c*) While still hot the feeds are transferred to a refrigerator where they remain until just before use. A day's supply of feeds is prepared at a time.

We believe that it is wiser to allow for possible contamination of milk-feeds with coliform organisms than to place undue reliance on techniques intended to prevent their entry.

As important as the limitation of cross-infection within a ward is the prevention of entry of specific organisms to that ward. Unfortunately this is not easy to achieve. However carefully new cases are scrutinised, there is obviously no way of detecting in the admitting-room either a symptomless carrier or a child incubating coliform diarrhœa. Preliminary surveillance for a few days after admission in a separate observation unit would doubtless lead to the recognition and exclusion of most of these occult infections. The real difficulty arises with the so-called intermittent excreter, whose potential infectivity may escape detection in spite of a short period of initial bacteriological screening.

Smith and Galloway (1953) and Todd and Hall (1953) have observed the reappearance of specific types of *Esch. coli* in the stools after their temporary disappearance under oral antibiotic treatment. We have traced similar bacteriological relapses in infants who have yielded, after chemotherapy, series of negative swabs. These relapses are often symptomless and sometimes intermittent. Factors other than chemotherapy might have contributed to our findings concerning intermittent excretion. One of these factors was our use of swabs, since routine examination of fæces might have yielded positive results with greater frequency. Another factor was sampling error, the effect of which is greatest when the organisms being looked for are present in numbers approximating to the threshold of the isolation technique. Thus, for the isolation of specific types of *Esch. coli* we have to rely on random sampling of colonies developing from necessarily small inocula on a relatively non-selective culture medium. If refinements in isolation technique had been available to us, similar to those which have been applied during the last two decades in the isolation of salmonellæ, many of our observed gaps in excretion might have been bridged. Intermittent culture findings identical with those we have observed could have resulted from sampling error alone in series of specimens containing relatively small numbers of O,55, though it is almost certain that fluctuation in these numbers was also contributory to our findings.

In view of the technical limitations it is perhaps surprising that O,55 was isolated from so high a proportion of our cases of hospital gastro-enteritis. Had equivalent inocula from a like series of infants infected with *Shigella sonnei* been similarly plated on MacConkey's medium alone, we know from previous experience that we should have obtained more failures of isolation. We believe that the explanation for this lies in the greater ability of specific types of *Esch. coli* to colonise the gut of the artificially fed infant, and to set up conditions favourable to their continued excretion in relatively far greater numbers than obtain with *shigellæ* and *salmonellæ*. We also believe, with Rogers (1951a), that this is the reason why spread of coliform diarrhœa among infants is so very much more difficult to control than spread of other bowel infections.

We have mentioned a temporary cessation of excretion of a specific type of *Esch. coli* which may follow chemotherapy. Our limited experience of intermittent excreters of O,55 has been compatible with a hypothesis which we postulate tentatively—i.e., that factors which disturb the balance between a specific type of *Esch. coli* and its infant host in favour of the host predispose to the state of intermittent excretion. Factors we have observed other than chemotherapy which have fitted in with this

generalisation are the transition of an infant to a less susceptible age-group, and feeding with breast-milk.

Our experiences with intermittent excreters of O,55 have led us during the last year to a further modification of the system of admission to the infants' ward. Once a child has been in the gastro-enteritis unit he is readmitted to that unit for all subsequent illnesses of infancy requiring hospital treatment, whatever their nature, irrespective of the findings in the child's swabs during the first visit. For similar reasons we do not discharge infants from the gastro-enteritis unit to nurseries and convalescent homes; nor are we misled by several negative rectal swabs, particularly after a course of chemotherapy. If an infant cannot be returned home, we try to place it in an institution where there are facilities for strict isolation, or, failing that, in a foster home where there are no other children of susceptible age.

The part played by institutions—and in particular our own hospital—in the spread of coliform diarrhœa has been considered elsewhere in this report. Because of this risk of dissemination of infection an enteritis follow-up clinic is now conducted in a building outside the precincts of the hospital, and parents are advised of the undesirability of taking potentially infected infants to doctors' consulting-rooms, welfare clinics, and our own outpatient department. The finding that among the 31 infants excreting O,55 on admission there was a history of recent institutional contact in 19 was not unexpected. The admission of babies from residential nurseries, convalescent homes for infants, and other hospitals obviously requires careful consideration, and there is a real need for some means of preliminary isolation to establish, so far as is possible, freedom from infection before their introduction to a susceptible community in an open ward.

A crucial remaining question to which an answer must be given is whether or not O,55 was a causal agent of gastro-enteritis within our survey population. We are satisfied that it was—for the following reasons:

There is a striking parallel in the decline of clinical infections during period III with the decline of bacteriological infections with O,55. Each of the two outbreaks, one which continued through the whole of period II, the other occurring in January, 1953, followed the introduction of O,55 into the ward, and each outbreak was followed by a secondary wave of infection in the gastro-enteritis unit. The transfer of an excreter of O,55 to another hospital was also followed by an outbreak of gastro-enteritis in that hospital. The isolation-rates of O,55 from infants with gastro-enteritis shown in the table speak eloquently enough for themselves. It should be pointed out here that the single infant within the survey population from whom O,55 was not isolated during period II was infected with O,111. The 2 sporadic cases during period III from which specific types of *Esch. coli* were not isolated could not be distinguished clinically from mild cases of hospital gastro-enteritis, but it is noteworthy that neither of these 2 cases transmitted infection to any of its ward associates.

The fact that O,55 was present in the fæces of many infants who did not satisfy our criteria for the diagnosis of gastro-enteritis carries no conviction as an argument against its pathogenicity since, as Smith (1953) has already pointed out, symptomless excreters may often be met with in outbreaks of infection caused by *Shigella sonnei* and other intestinal pathogens. A last refuge of the opponents of the bacterial hypothesis of hospital gastro-enteritis is the argument that these specific types of *Esch. coli* are riding on the backs of viruses or other unascertained causes of the disease which promote conditions favourable for the multiplication of specific types of *Esch. coli*. This we feel is begging the question, and, if advanced in the face of the published evidence, the same argument might equally apply to many bacterial diseases. The fact remains that the presence of specific types of *Esch. coli* in the fæces or rectal swabs of cases or contacts of hospital gastro-enteritis has in our experience proved a singularly reliable warning of trouble.

Summary

A survey has been made of infantile gastro-enteritis acquired in the infants' ward of a children's hospital during the six years from September, 1947, to August, 1953. Morbidity and mortality figures are presented.

A bacteriological study covers the period from April, 1950, to August, 1953. One or other of two specific types of *Esch. coli*—O group 111: B,4 and O group 55: B,5—was isolated from 74 of the 77 cases occurring during this period. Conclusions are drawn about the pathogenic rôle of these organisms.

Factors which influence the epidemiology of infantile gastro-enteritis are considered, and measures which were effective in limiting the spread of this disease in the infants' ward are described and discussed.

Our thanks are due to Dr. E. D. Scott and Dr. W. Mestitz for access to their cases; to Dr. Joan Taylor and Dr. K. B. Rogers for their helpful criticisms and advice; and to Miss D. A. Scott for invaluable help given in the preparation of charts to which we have referred during the compilation of this report.

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LATE RESULTS OF TREATMENT IN MYOCARDIAL INFARCTION

EFFECT OF SHORT-TERM ANTICOAGULANT THERAPY ON THE MORTALITY AT ONE YEAR

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ANTICOAGULANTS are now extensively used in the treatment of acute myocardial infarction, and published series of cases (e.g., Tulloch and Gilchrist 1950, Wright et al. 1954) have shown that their use reduces the mortality during the patient's stay in hospital—i.e., during the first four to six weeks after the infarction. However, the effect of this short-term therapy on the late mortality has not been studied.

This report deals with 100 patients with acute myocardial infarction, all of whom received anticoagulant therapy during their stay in hospital and were followed up for a year after the onset. Previous controlled series have shown such striking advantages in anticoagulant therapy that we think it unjustifiable to withhold this treatment in a proved case, and therefore there is no control series of untreated cases in this study.

We hope that this report of the late results of short-term treatment in recent infarction will be of value in assessing the results of maintained outpatient anticoagulant therapy which is now on trial in this hospital.

* In receipt of a grant from the Secretary of State for Scotland.

Description of Cases

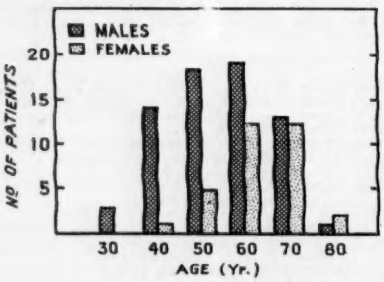
Selection of Patients

All patients admitted to the medical wards of Maryfield Hospital, Dundee, between October, 1949, and December, 1952, in whom a diagnosis of acute or recent myocardial infarction was made were considered for inclusion in the study. Patients dying within the first twelve hours after admission to hospital were excluded, as were those with contra-indications to anticoagulant therapy—e.g., any coexisting condition predisposing to hæmorrhage, such as ulcerative lesions of the alimentary tract. No patient in whom the onset of infarction had occurred more than fourteen days before admission was included.

When cases had been rejected for the reasons stated, there remained 103 patients, of whom 3 had to be excluded because of failure to trace them a year from the date of their admission to hospital.

Analysis of Series

The ratio of males to females was 2·1 : 1, which shows a slightly larger proportion of females than in most recent reports (Wright et al. 1948, Doscher and Poindexter 1950, Papp and Smith 1951). The ages ranged from 35 to 85 years, the average for the group being 59·8. The average age of males was 56·5 and of females 66·5. The age and sex distribution is shown in the accompanying figure.



Distribution of cases as regards age and sex.

The average age for all the patients, and the later age-incidence in women, are in conformity with most other published reports—e.g., Willius (1936) and Rathe (1942).

The interval between the onset of infarction and admission to hospital was less than forty-eight hours in 62 cases and between forty-eight hours and fourteen days in 38 cases.

Electrocardiography was carried out in every case, and the characteristic changes of acute myocardial infarction were present in 85 patients. In 15 the electrocardiograms did not show definite evidence of infarction, but in these cases the diagnosis was made with reasonable confidence on clinical grounds.

In 81 patients the attack of myocardial infarction was their first. A history of one previous attack was obtained in 17, and of two previous attacks in 2 patients.

Severity of Illness

The classification of Russek et al. (1951b) has been adopted in grouping cases as "good risk" or "poor risk." Good-risk patients have had no previous myocardial infarction and show none of the following: persistence of pain or shock, evidence of cardiac failure, significant enlargement of the heart, arrhythmia, gallop rhythm, diabetic acidosis, or gross obesity. Poor-risk patients are those who show one or more of these unfavourable signs. This classification was made in retrospect according to the details of examination and history noted on the day of admission.

In this series there were 51 poor-risk patients and 49 good-risk patients. The distribution of good-risk and poor-risk cases as regards age and sex is shown in table I.

Apart from the later age-incidence in women, which we have already noted (see figure), the most interesting finding in this table is the proportion of good-risk and poor-risk cases in patients over 60 years of age. There is a preponderance of poor-risk cases in females in this group, whereas males show a slight excess of good-risk cases. Russek et al. (1951a) also found a greater proportion of poor-risk cases in patients aged over 60, but they did not give separate figures for males and females.

TABLE I—DISTRIBUTION OF CASES AND MORTALITY-RATES ACCORDING TO SEVERITY OF ILLNESS

Severity of illness	Age (yr.)				Total		Total no. of cases	Mortality	
	Less than 60		More than 60						
	M	F	M	F	M	F		At 1 mo.	At 1 yr.
Good risk ..	19	4	18	8	37	12	49	2 (4·0%)	5 (10·2%)
Poor risk ..	16	2	15	18	31	20	51	7 (13·7%)	13 (25·5%)
Total ..	35	6	33	26	68	32	100	9%	18%

Treatment

Complete rest in bed was enforced for from four to six weeks, after which activity was gradually increased under the guidance of a physiotherapist. Most patients received a light diet of 1500–1800 calories but, except in gross obesity or diabetes, no strict dietetic régime was ordered.

Analgesics and sedatives were administered when necessary, and quinidine or procaine amide was used when specifically indicated in the treatment of arrhythmias. Digitalis was given only in the presence of severe or persistent congestive failure.

Heparin was administered by intermittent intravenous injection for from two to five days to 73 patients. All the patients received ethyl biscoumacetate ('Tromexan'), the dosage of which was carefully controlled by the one-stage clotting-test (Quick et al. 1935). Where heparin was used initially, tromexan therapy was begun at least twenty-four hours before the heparin injections were stopped.

Excluding patients dying in hospital, the duration of anticoagulant treatment was four weeks or more in 56 cases, three or four weeks in 25 cases, and less than three weeks in 10.

Hæmorrhagic complications, requiring the cessation of anticoagulant therapy, occurred in 5 patients, of whom 2 had hæmaturia, 2 had hæmatemesis, and 1 had hæmoptysis.

Control of Therapy

Stirling and Hunter (1951) found that an initial single dose of 1200 mg. of ethyl biscoumacetate in the first twenty-four hours was less effective than four doses of 300 mg. given six-hourly. At the start of therapy each patient received 300 mg. six-hourly until the prothrombin activity was 10–20% of normal, which was regarded as the therapeutic range for ethyl biscoumacetate, and corresponded to a one-stage time of 25–40 sec.—i.e., two or three times that of the normal control. This is similar to the prothrombin level adopted in most other series. The prothrombin activity was estimated daily during the first seven to ten days, and according to the individual levels of activity recorded the dosage of ethyl biscoumacetate for the succeeding twenty-four hour period was prescribed. It was found with most patients that, after the maintenance dose had been ascertained, measurements of prothrombin activity on alternate days were adequate for safe control. In conformity with most reports on the use of ethyl biscoumacetate, we found that the maintenance dose varied widely in different patients, from 100 mg. to 1200 mg. daily, but that it usually remained relatively steady in any one patient.

It is the practice in this hospital that one member of the medical staff of the Therapeutics Unit is responsible for the control of anticoagulant therapy. Thus the same person who performs each one-stage test subsequently prescribes the anticoagulant. We believe that this unity

of responsibility and control is important and increases the efficacy and safety of anticoagulant therapy.

Except for the first 14 cases, which were controlled by Dr. Margaret Pearson, we have been responsible for all the prothrombin estimations and for controlling the dosage of ethyl biscoumacetate.

Follow-up

62 patients attended the follow-up clinic a year after the date of their admission to hospital and were examined by one of us. Information about the remainder of the patients was obtained by letter from the patient, his relatives, or his doctor.

Results

We defined early mortality as the death-rate in the first four weeks after the onset of infarction. As stated above, patients dying within twelve hours of admission to hospital were not included.

The early mortality in this series was 9%, and a further 9% of patients died during the remainder of the first year; thus the total mortality at the end of a year was 18%. The early and late mortalities, in relation to severity of illness, age, and sex, are shown in tables I–III.

Table II shows that the mortality is greater in the older patients, as is generally accepted; but males and females have almost the same early and late mortality-rates (table III), in spite of the greater proportion of poor-risk cases among the females. As was expected,

TABLE II—MORTALITY-RATES IN RELATION TO AGE

Age (yr.)	No. of patients	Deaths in 4 weeks	Deaths in 1 year
Less than 60 ..	41	0	5 (12·2%)
More than 60 ..	59	9	13 (22%)

poor-risk cases had a considerably higher mortality, both early and late, than had good-risk cases.

Thrombo-embolic Episodes and Further Infarction

The incidence of further myocardial infarction and other episodes of thrombosis and embolism is shown in table IV. The thrombo-embolic episodes included embolism of brachial, mesenteric, and pulmonary arteries, cerebral vascular accidents, and deep venous thrombosis. When further myocardial infarction and other instances of thrombo-embolism are taken together, the incidence of such complications during the first month was 12%, and the total incidence after a year was 26%.

Discussion

The early prognosis in myocardial infarction has been the subject of many studies, in which widely divergent mortality-rates have been reported. The true mortality cannot be obtained from a study of patients treated in hospital, because such patients form a selected group of all cases (Schnur 1953). Many mild cases are treated at home; also many attacks prove rapidly fatal, before the patient can be admitted to hospital (Morris et al. 1953). High mortality-rates have been reported when cases proving rapidly fatal were included in the series (Newman 1946, Yater et al. 1948).

It is evident that the series of cases studied have not been comparable, varying in the criteria for selection and in their composition as regards age, sex, and severity of illness—all factors which influence the mortality-rate. Most reports show that increasing age worsens the prognosis (Master et al. 1939, Rosenbaum and Levine

TABLE III—MORTALITY-RATES IN RELATION TO SEX

Sex	No. of patients	Mortality at 4 weeks	Mortality at 1 yr.
Males	68	6 (8·8%)	12 (17·6%)
Females ..	32	3 (9·4%)	6 (18·7%)
Total	100	9%	18%

TABLE IV—FURTHER MYOCARDIAL INFARCTIONS AND OTHER THROMBO-EMBOLIC EPISODES

—	No. of incidents			
	Within 1 mo.		Within 1 yr.	
	Total	Deaths	Total	Deaths
Further myocardial infarction ..	6	3	18	8
Other episodes of thrombo-embolism	6	2	8	3

1941, Russek et al. 1951a). It is generally stated that the mortality is higher in women (Mintz and Katz 1947, Sigler 1951), but this may be associated with the higher age-incidence of myocardial infarction in women (Willius 1936, Master et al. 1939).

First attacks appear to have a better prognosis than subsequent attacks (Conner and Holt 1930, Rathe 1942, Doscher and Poindexter 1950), and there is no doubt that mild attacks have a better prognosis than severe attacks (Papp and Smith 1951, Russek et al. 1951b). As the peak mortality is in the first week (Morris et al. 1952), the hospital mortality-rate is further influenced by the interval between the onset of infarction and admission.

Notwithstanding all these variable factors, most workers report an early mortality in the range of 20–40% for an unselected hospital series of cases of myocardial infarction treated without anticoagulants (Cooksey 1935, Fisher and Zukerman 1946, Mintz and Katz 1947, Wright et al. 1948, Billings et al. 1949, Russek et al. 1951b, Pearson 1953).

Several controlled series have now been published, showing the reduction in the early mortality following anticoagulant therapy (Peters et al. 1946, Greisman and Marcus 1948, Schilling 1950, Tulloch and Gilchrist 1950, Holten 1951, Loudon et al. 1953, Wright et al. 1954). In the present series the early mortality of 9% confirms that a relatively low early mortality can be obtained using anticoagulants.

Russek et al. (1951b) classified their cases of myocardial infarction as good-risk and poor-risk according to the criteria which we have already cited, and they reported that the early mortality was 2·45% in good-risk cases and 44·5% in poor-risk cases, all treated without anticoagulants. They believe that anticoagulant therapy is indicated only in poor-risk cases, because the low mortality of good-risk cases cannot be further reduced by this treatment. Furman et al. (1953), as the result of a controlled study, have also decided that good-risk cases should not receive anticoagulants. Wright et al. (1954) found a mortality of less than 2% in good-risk cases both in a control group and in a group treated with anticoagulants. The difficulty in deciding on the day of admission whether a patient should be classed as a good or a poor risk is emphasised by Wright (1953), who is not in favour of restricting anticoagulant therapy to patients who are seriously ill. Moreover Wright (1953) shows that, although the early mortality of good-risk cases is not influenced by anticoagulant therapy, yet the incidence of thrombo-embolic complications and subsequent morbidity is less in anticoagulant-treated than in control patients, even in the good-risk category. In the present series the early and late mortality-rates are more than twice as great in poor-risk as in good-risk cases (table I). Our findings support the claim that this classification has practical value in assessing prognosis, but we have not restricted the use of anticoagulants to poor-risk cases.

Very few reports have been published on the mortality-rate at a year after an acute myocardial infarction, and it has not been shown to what extent the late mortality is reduced by anticoagulant therapy during the acute illness. In a study of 488 patients Katz et al. (1949)

TABLE V—MORTALITY-RATES IN FIRST MONTH AND IN LAST ELEVEN MONTHS OF FIRST YEAR

Reference	Early mortality	Total mortality at 1 yr.	Mortality during last eleven mos. of first yr.
Katz et al. (1949) ..	22%	45%	23%
Fisher and Zukerman (1946)	27%	48%	21%
Present series	9%	18%	9%

reported that the mortality at a year was 45%. Fisher and Zukerman (1946) reported the mortality at a year as 48%. A lower figure was recorded by Bland and White (1941), who found the mortality to be 34%; their series was composed entirely of patients seen in private practice and it contained a higher proportion of males (84%) than did most other series. All the aforementioned reports of death-rates at a year were based on patients treated without anticoagulants.

The total mortality at a year in this series is 18%: this figure is considerably less than any reported mortality at a year when patients were treated without anticoagulants. To what extent is this low figure for late mortality caused by the reduction in mortality during the first month, and to what extent, if any, is it brought about by a diminished death-rate during the remainder of the year? This problem assumes great importance in assessing the results of anticoagulant therapy in myocardial infarction. Does the administration of anticoagulants for a month have any influence on the prognosis during the succeeding eleven months after treatment has been stopped?

The death-rate during the latter eleven months of the first year has been calculated from the early and late mortality figures for two published series and for the present series (table v). The early mortalities of the two previously reported series are similar to most other reports of cases treated without anticoagulants, and the early mortality of the present series is within the usual range for anticoagulant-treated cases; so it is reasonable to suppose that none of these series is of an atypical composition. Thus a comparison can be made between the calculated death-rates.

These figures show not only that the early mortality and total mortality at a year are much less in the present series but also that the proportion of patients dying during the latter eleven months of the first year (after anticoagulant therapy was stopped) is considerably less in the present series than in the previous series where anticoagulants were not used. This suggests that a patient who has been treated with anticoagulants and has survived for a month has a better prognosis than a patient who has survived the acute illness without anticoagulant therapy. Much more evidence is required to establish this point, and the long-term effects of anticoagulant therapy should be further investigated.

It is important to discover whether the late mortality could be further reduced by following up the treatment of the acute illness in hospital with long-term outpatient anticoagulant therapy. This is at present being investigated.

Summary

The main purpose of this study was to determine the mortality in myocardial infarction at one year after short-term anticoagulant therapy, because little has been reported of the late results of such treatment.

A hundred patients with acute myocardial infarction have been followed up for a year from the date of their admission to hospital. Anticoagulant therapy was used in all of them during their stay in hospital, and the control of this treatment is described in detail.

The hospital mortality in the first month after the onset of infarction was 9%, deaths within the first twelve hours after admission being excluded. The total mortality at a year was 18%. The death-rates are expressed in relation to sex, age, and severity of illness.

Previous reports of the mortality after myocardial infarction are briefly reviewed.

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THE MECHANICAL ASPECTS OF ARTIFICAL PNEUMOTHORAX

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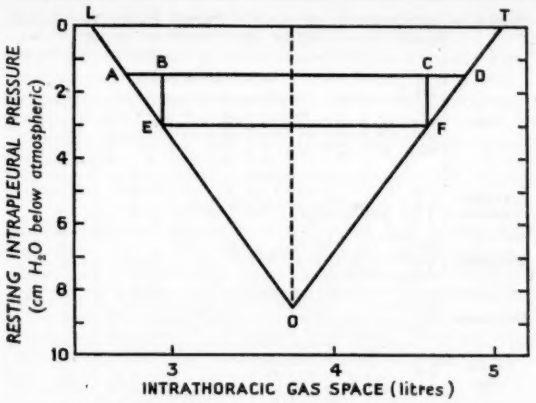
IMPROVEMENTS in the methods of measuring intrathoracic pressure changes (Dornhorst and Leathart 1952, Fry et al. 1952) have promoted further investigation of the mechanical properties of the lungs. Our starting-point in this field has been the observations of Christie and his collaborators many years ago and more recently (Christie and McIntosh 1934, McIlroy 1952, McIlroy and Christie 1952, 1954, McIlroy et al. 1954, Marshall et al. 1954). The principal subject of their study has been the work of breathing, and this has involved a close analysis of the elastic and non-elastic elements of the resistance to breathing offered by the lungs. We have investigated the elastic properties of the chest wall in a few patients who had artificial pneumothorax induced as part of the treatment for pulmonary tuberculosis. (For the purposes of this report the chest wall will be taken to include the diaphragm as well as the thoracic cage and its muscles.)

Christie and McIntosh (1934) showed that, during the induction and the refilling of an artificial pneumothorax, the volume of air expelled from the lungs was less than the volume injected into the pleural cavity, the excess being taken up by the expansion of the chest walls.



Pressure-volume diagram of artificial pneumothorax.

In our investigations we repeated their work and included estimates of the volume of the pneumothorax as well as measurements of the functional residual capacity of the lungs. We have devised a diagram which illustrates our results and is helpful in their interpretation (see figure).

Methods

Observations were made on patients who had no radiological or other evidence of pleural thickening or fixation and who were accustomed to receive about 500 ml. of air at each refill. The patient was seated with his arms resting on a support placed in front of him at about chin level; this position facilitated spirometry and allowed the operator to introduce the needle used for administering the refill in the mid-axillary line, where most patients are accustomed to it. A Saugmann needle was used; this has a side-arm, which was connected to the apparatus used for giving the refill and to a strain-gauge manometer; a three-way tap allowed the needle to communicate with either of these independently. The hub of the needle has a tap incorporated in it through which it is possible to sample the intrapleural gases without interfering with the other apparatus.

When the patient was comfortably seated he was instructed to breathe into a Knipping spirometer filled with air; oxygen was run into the circuit continuously at a rate equal to his consumption of oxygen. A level spirogram was thereby obtained from which it was easy to read off the volume changes of the lungs during the refilling of the pneumothorax. A second strain-gauge manometer was attached to a manifold situated in the mouth-piece of the spirometer. The output of this was electrically opposed to that of the manometer communicating with the pleura so that a combined signal was produced, giving the pressure gradient at any instant between the mouth and the intrapleural space. This signal was displayed on a cathode-ray oscilloscope and could be recorded photographically. The particular measurement we were interested in was of intrapleural pressure at the end of a normal breath; this is the resting level of intrapleural pressure and corresponds to the resting lung volume or functional residual capacity.

The needle was introduced into the pleural cavity, and after a few minutes' quiet breathing the intrapleural pressure swing was recorded, and the corresponding breaths, recorded on the spirogram, were marked. A sample of intrapleural gas was taken through the needle into a lightly oiled glass syringe; this was transferred to a glass bulb, where it was kept over mercury until required for analysis. Pure nitrogen was used to refill the pneumothorax; it was measured from the refill apparatus, whose volume calibrations had previously been checked by displacement of water. The volume of gas expelled from the lungs as result of the introduction of the nitrogen into the pleura was observed on the spirogram as it was expelled; it was measured accurately afterwards. The pressure swings were again recorded, and another sample of intrapleural gas was taken. After a short rest the functional residual capacity of the patient's lungs was measured by McMichael's (1939) method using closed-circuit dilution of helium.

Knowing the volume of nitrogen introduced into the pneumothorax and the percentage composition of the intrapleural gases before and after administration we could calculate the initial and final volumes of the pneumothorax. The volume of the lungs in the initial resting respiratory position was found by adding to their final volume the volume of gas expelled from them during the procedure, as read from the spirogram. The difference between the volume of gas administered and the volume change of the lungs gave the increase in volume of the chest walls.

Results

Five experiments have been carried out. Since the results in all were similar, it is only necessary to consider one experiment and this is illustrated in the figure. In this diagram the point E shows the initial volume of the lungs at the observed level of intrapleural pressure, and the distance EF represents the volume of the artificial pneumothorax before refill. Similarly the point A and the line AD represent the conditions after the refill. Straight lines have been drawn through AE and DF which meet at O and cut the volume axis at L and T; these depict the *compliance* of the lungs and chest walls respectively—i.e., they show by how much the volume of each of these structures is altered by unit change in intrapleural pressure. In the case illustrated the compliance of the lungs is 0·14 litre per ml. of water, and that of the chest wall 0·15. In other cases the ranges found for compliance were 0·12–0·21 litre per ml. of water for the lungs and 0·07–0·21 for the chest walls. These figures are in general agreement with those found by other workers (Mead and Whittenberger 1953, Ferris et al. 1952, Otis et al. 1950).

Discussion

In the figure the two lungs are considered as a single unit, and it is assumed that the pressure read in one pleural cavity is the same as that in the other. The triangular area LOT is then a pressure-volume-diagram of the pleural cavity as a whole. The base-line of the diagram LT represents the volume of air which the pleural cavity would hold if it were at atmospheric pressure. At this pressure the lungs are not completely empty of air, a fact which is common knowledge among those who are familiar with artificial pneumothorax therapy. The volume shown at the point T and at any other point along the line OT we call the *total intrathoracic gas volume* because it does not include any of the capacity of the chest wall filled by tissue. It is seen to be composed of two parts—the volume of gas in the lungs and that in the pneumothorax. If air is withdrawn from the pleura when the intrapleural pressure is atmospheric, the pressure falls, the lungs gradually expand, and the chest walls collapse until their pleural surfaces are in contact—the position in the intact thorax. This is illustrated at point O, whose coördinates are the functional residual capacity and intrapleural pressure which would have been found before the induction of the artificial pneumothorax. At any level of intrapleural pressure between O and atmospheric pressure a line such as AD may be drawn between OL and OT which represents the volume of the pneumothorax which could exist at that pressure. The resting volume of the lungs is thus seen to be maintained by the opposed elastic stresses of the lungs and the chest walls. In healthy people and in most patients this lung volume is kept remarkably constant; it is difficult to alter voluntarily to a different constant level for any long period, because the mechanical balance between

the two stresses has to be modified by a constant amount of muscular activity superimposed upon the rhythmic activity required for breathing.

The results we have obtained cannot indicate the true shape of the lung and chest-wall lines, OL and OT. In the case of the lung line it is possible to obtain a series of points which lie along a line which is very nearly straight except at pressures near to atmospheric, where it is usually inflected upwards, indicating a fall in compliance. At least part of this departure from linearity is due to trapping of air beyond respiratory bronchioles which, being thin-walled and unsupported by cartilage, are easily collapsed at these levels of intrapleural pressure. The chest-wall line also seems to be nearly straight in the range of pressures considered here (Ferris et al. 1952).

Summary

Observations of the pressure-volume relationships which prevail in the lungs and pleural cavities of patients who have an artificial pneumothorax have been used to calculate values for compliance of the lungs and chest walls.

In the cases examined these were of similar magnitude.

A diagram is described which helps in the interpretation of the findings.

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EVALUATION OF OCCULT-BLOOD TESTS ON FÆCES

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TESTS for the presence of occult blood in fæces form an important part of the investigation of anæmia and gastro-intestinal disease. Positive tests may point to an ulcerative lesion in the gastro-intestinal tract long before such a lesion can be demonstrated clinically or radiologically. If it could be shown that dietary restriction was not necessary before doing these tests, they would undoubtedly be used more often. Such dietary restriction, and the withholding of iron therapy for several days before the tests, discourage practitioners from doing them.

Blood which is swallowed or is derived from a gastro-intestinal lesion is evacuated in the fæces partly as acid hæmatin and partly as hæmatoporphyrin. The chemical tests for occult blood depend on the conversion of a substance with little or no colour, such as guaiac, benzidine, or amidopyrine, into a coloured substance when oxidised by hydrogen peroxide in the presence of an oxygen carrier, such as hæmatin. Thus hæmoglobin or chlorophyll in the diet may give a positive result; but this depends on the sensitivity of the test and on the amount of these oxygen-carrying substances in the diet.

Medicinal iron, which is not an oxygen carrier, should not produce a positive result in any of the tests for occult blood; but there remains some difference of opinion concerning the effect of iron therapy on these tests. Some workers (Burger 1934, Hutchison and Hunter 1949, Price 1950) believe that medicinal iron gives a positive result with the benzidine test, but not with the guaiacum test. On the other hand, Hughes (1952) has shown that a solution of ferrous sulphate gives a positive result with the guaiacum test but not with the benzidine and Gregersen tests, and that a mixture of iron and ammonium citrate does not give a positive result with any of the tests. Bell (1923) and Bailey (1950) recommend that iron should not be given during the period of investigation with any of the occult-blood tests. Todd et al. (1948) believe that medicinal iron does not give a positive result with the benzidine test, and Needham and Simpson (1952) have shown that false-positive results are not produced by taking ferrous sulphate or iron and ammonium citrate in either the benzidine or the Gregersen test.

TABLE I—SENSITIVITY OF OCCULT-BLOOD TESTS TO GRADED DILUTIONS OF THREE SPECIMENS OF BLOOD

Test	Hb (g. per 100 ml.)	Dilutions of blood										
		1/500	1/1000	1/2000	1/4000	1/8000	1/16000	1/32000	1/64000	1/128000	1/150000	1/180000
Amido-pyrine	13·9	..	..	++	++	+	+	N	..	..	..	..
	9·6	..	++	++	+	N	..	..	..	..	..	..
	5·3	+	+	N	..	..	..	..	..	..	..	..
Benzidine	13·9	..	..	++	++	N	..	..	..	..	..	..
	9·6	..	++	++	N	..	..	..	..	..	..	..
	5·3	+	N	..	..	..	..	..	..	..	..	..
Gregersen	13·9	..	..	++	++	++	++	++	++	+	+	N
	9·6	..	++	++	++	++	+	+	N	..	..	..
	5·3	++	++	+	+	+	N	..	..	..	..	..
Guaia-cum	13·9	..	..	++	N	..	..	..	..	..	..	..
	9·6	..	+	+	N	..	..	..	..	..	..	..
	5·3	+	N	..	..	..	..	..	..	..	..	..

The recommendations for dietary preparation before doing the tests for occult blood also vary. Bell (1923), French and Douthwaite (1945), Harrison (1947), Hutchison and Hunter (1949), Bailey (1950), Price (1950), and Payne (1954) recommend that the diet should not contain meat or green vegetables; and Chamberlain (1952) recommends a farinaceous diet. Beaumont (1953) does not advise dietary preparation; but if the result is positive the test should be repeated after omitting meat, fish, and green vegetables from the diet. Needham and Simpson (1952) have concluded from a review of published reports that the benzidine test is sufficiently sensitive to be affected by a normal diet, and that the dietary restriction which accordingly must be imposed renders the test of very limited value. On the other hand, they have shown that the Gregersen test does not give positive results with a normal diet, unless it contains black-pudding or liver. Hughes (1952) has found, on testing the fæces of patients who were on a normal diet and in whom there was no evidence of gastro-intestinal bleeding, that 38% of the results were positive with the guaiacum test, 87·3% were positive with the benzidine test, 89·3% were positive with the phenolphthalein test, and only 8% were positive with the Gregersen test. Similar results were obtained by Bell (1923) with the guaiacum and benzidine tests.

Previous workers have shown, therefore, that the results of the Gregersen test are unaffected by normal diet and medicinal iron, but opinions differ about the preparation for the other occult-blood tests. The present study was undertaken in order to investigate the effects of ordinary diet and medicinal iron on the results of the amidopyrine, benzidine, Gregersen, and guaiacum tests and also to determine their relative sensitivity.

Methods

Amidopyrine Test

A fæcal suspension was prepared by boiling a small amount of fæces, about the size of a pea, with 5 ml. of distilled water, and then thoroughly cooling it.

1 ml. of this suspension was placed in a test-tube, and to this was added 1 ml. of 50% acetic acid and 1 ml. of 5% amidopyrine in methylated spirit. Finally, 1 ml. of hydrogen peroxide in 10-volumes strength was added. A positive result was indicated by a blue colour developing within 2 minutes. A pale blue colour was recorded as "weakly positive" and a well-developed blue colour as "positive."

Benzidine Test

1 ml. of fæcal suspension prepared as for the amidopyrine test was placed in a test-tube, and to this was added 2 ml. of 3% benzidine in glacial acetic acid. Then 1 ml. of hydrogen peroxide in 10-volumes strength was added to the tube, accompanied by vigorous shaking. The test was regarded as positive if a blue colour developed at once. A greenish-blue colour was recorded as "weakly positive," and a blue colour as "positive."

Gregersen Test

A reagent was made by dissolving a prepared powder containing 0·2 g. of barium peroxide and 0·025 g. benzidine in 5 ml. of 50% glacial acetic acid. 3–4 drops of the reagent were run on to a thin smear of fæces on a filter-paper, and the presence of a blue colour indicated a positive result. The result was recorded as "positive" if the colour appeared within 15 seconds, "weakly positive" if it appeared within 16–30 seconds, and "negative" if it appeared after 30 seconds. Since a blue colour sometimes develops within 30 seconds if the reagent is dropped on to a clean, dry filter-paper, care was taken to take note of a blue colour only if it developed at the site of the fæcal smear and spread outwards from it.

Guaiacum Test

To 1 ml. of the fæcal suspension in a test-tube was added 1 ml. of 1% guaiacum gum in methylated spirit, and 1 ml. of hydrogen peroxide in 10-volumes strength. A green colour resulting was recorded as "weakly positive," and a blue colour as "positive." The test was regarded as positive only if the colour developed within 2 minutes.

The colour reactions in all the tests have been graded as follows: N = "negative"; + = "weakly positive"; ++ = "positive."

Investigation

Tests on Iron

The four occult-blood tests were made on the following solutions of inorganic iron: (*a*) 10% solution of ferrous sulphate; (*b*) 10% solution of ferric chloride; (*c*) 25% solution of mist. ferri et ammon. cit. (*N.F.*). The results of all these tests were negative.

Tests on Oxalated Blood

The in-vitro sensitivity of the tests was estimated by testing serial dilutions, in distilled water, of three samples of oxalated blood, containing 13·9 g. Hb, 9·6 g. Hb, and 5·3 g. Hb per 100 ml. The results are shown in table I.

TABLE II—RESULTS OF OCCULT-BLOOD TESTS ON FÆCES OF SEVEN HEALTHY SUBJECTS AFTER DRINKING A MEASURED AMOUNT OF BLOOD

Case no.	Test	Amount of blood drunk (ml.)			
		5	8	10	13
1	Amidopyrine	N	++	+	++
	Benzidine	N	++	++	++
	Gregersen	N	N	N	++
	Guaiacum	N	+	N	++
2	Amidopyrine	N	N	+	+
	Benzidine	N	++	++	++
	Gregersen	N	N	N	+
	Guaiacum	N	N	N	+
3	Amidopyrine	N	+	..	..
	Benzidine	N	++	..	..
	Gregersen	N	+	..	..
	Guaiacum	N	+	..	..
4	Amidopyrine	+	+	..	..
	Benzidine	+	++	..	..
	Gregersen	N	+	..	..
	Guaiacum	+	+	..	..
5	Amidopyrine	+	+	..	..
	Benzidine	+	++	..	..
	Gregersen	N	++	..	..
	Guaiacum	+	+	..	..
6	Amidopyrine	N	N	++	..
	Benzidine	N	N	++	..
	Gregersen	N	N	+	..
	Guaiacum	N	N	++	..
7	Amidopyrine	N	++	..	..
	Benzidine	N	++	..	..
	Gregersen	N	++	..	..
	Guaiacum	N	++	..	..

Tests on Fæces after Ingestion of Blood

The amount of blood which, when taken by mouth, produced a positive occult-blood test in the fæces was estimated in seven healthy young men. The specimens of blood which were consumed contained between 14·8 g. and 11·8 g. Hb per 100 ml. A negative occult-blood test was obtained on one specimen of fæces from each subject before consuming the blood, and each specimen of fæces obtained during the three days after consuming the blood was tested. The results are shown in table II, in which the positive results recorded are from the specimen of fæces which contained the most blood. 5 ml. of blood did not produce a positive Gregersen test, and produced a positive result with the other three tests in only two subjects. On the other hand, 8–10 ml. of blood produced a positive result in all benzidine and amidopyrine tests, in all but one guaiacum test, and in all but two Gregersen tests, which became positive with 13 ml. of blood.

TABLE III—RESULTS OF OCCULT-BLOOD TESTS ON PATIENTS TAKING ORDINARY HOSPITAL DIET AND PREPARATIONS OF IRON BY MOUTH

Test	Column I: Ordinary hospital diet (33 specimens from 10 patients)			Column II: Ordinary hospital diet and 6 tablets of fersolate daily (45 specimens from 11 patients)			Column III: Ordinary hospital diet and gr. 90 iron and ammonium citrate daily (50 specimens from 8 patients)			Column IV: Total of results from the 128 specimens in columns I–III		
	N	+	++	N	+	++	N	+	++	N	+	++
Amidopyrine ..	31 (94%)	2 (6%)	.. ..	33 (73%)	9 (20%)	3 (7%)	41 (82%)	7 (14%)	2 (4%)	105 (82%)	18 (14%)	5 (4%)
Benzidine	31 (94%)	.. ..	2 (6%)	33 (73%)	5 (11%)	7 (16%)	36 (72%)	6 (12%)	8 (16%)	100 (78%)	11 (9%)	17 (13%)
Gregersen	28 (85%)	2 (6%)	3 (9%)	35 (78%)	5 (11%)	5 (11%)	42 (84%)	5 (10%)	3 (6%)	105 (82%)	12 (9%)	11 (9%)
Guaiacum	31 (94%)	2 (6%)	.. ..	35 (78%)	8 (18%)	2 (4%)	39 (78%)	8 (16%)	3 (6%)	105 (82%)	18 (14%)	5 (4%)

Tests on Fæces from Patients Taking Ordinary Diet and Medicinal Iron

The investigation into the effect of diet and medicinal iron on the occult-blood tests was carried out on thirteen male hospital patients, who were not anæmic, and in whom gastro-intestinal bleeding could reasonably be presumed to be absent. Brushing of the teeth was not forbidden during the investigation. These tests were divided into three groups :

1. Thirty-three specimens of fæces were obtained from ten patients on an ordinary hospital diet who were not taking medicinal iron.

2. Forty-five specimens of fæces were obtained from eleven patients on an ordinary hospital diet who were taking two tablets of ferrous sulphate (' Fersolate ') (total gr. 6) three times daily.

3. Fifty specimens were obtained from eight patients on an ordinary hospital diet who were taking gr. 30 of ferri et ammon. cit. three times daily.

The results of the tests on these specimens are shown in table III. Although the proportion of positive results was higher in the groups of patients taking fersolate and ferri et ammon. cit., this appeared to be related to the higher consumption of black-puddings or liver in these groups. Of a total of ninety-seven positive results, sixty-two were obtained on fæces passed within three days of eating either black-pudding or, less usually, liver. The results of the tests after omitting these sixty-two results are shown in table IV.

TABLE IV—RESULTS OF OCCULT-BLOOD TESTS, OMITTING FÆCES PASSED WITHIN THREE DAYS OF EATING BLACK-PUDDING OR LIVER

Test	Negative	Weakly positive	Positive
Amidopyrine	105 (91%)	9 (8%)	1 (1%)
Benzidine	100 (91%)	7 (6%)	3 (3%)
Gregersen	105 (95%)	4 (4%)	1 (1%)
Guaiacum	105 (91%)	10 (8%)	1 (1%)

Discussion

The usual criticism of the benzidine and guaiacum tests for occult blood in fæces has been that they are too sensitive, and that without dietary preparation they commonly produce a false-positive reaction (Bell 1923, Hughes 1952). In addition, Bell (1923) showed that only 1 ml. of blood mixed with the food invariably produced positive reactions with the benzidine and guaiacum tests. The simplified benzidine test (Hughes 1952) and the modified Gregersen test (Needham and Simpson 1952) have been recommended recently because : (*a*) they were found to give very few false-positive reactions with fæces from patients on a normal diet ; (*b*) they were less sensitive than the benzidine and guaiacum tests with graded dilutions of blood ; and (*c*) more blood had to be introduced into the stomach to give a positive reaction —namely, 2 ml. with the simplified benzidine test and 2–5 ml. with the Gregersen test.

The present investigation on the effect of normal diet shows no appreciable difference between the amidopyrine, benzidine, Gregersen, and guaiacum tests. Black-puddings invariably produced positive results with all four tests, and liver occasionally produced positive results. Kidneys were not included in the diet, but probably they would also produce positive reactions. After omitting the results on the stools passed within three days of eating black-pudding or liver, we obtained negative results in 91% (benzidine, amidopyrine, and guaiacum tests) to 95% (Gregersen test) of specimens ; and of a combined total of four hundred and sixteen tests only six were positive. Four of these positive results were obtained from the same specimen, which was from a patient who was slightly constipated and had eaten black-pudding six days previously. Apart from black-pudding and liver, therefore, dietary restriction is not necessary ; and although the incidence of weakly positive reactions is 4–8%, the incidence of false-positive reactions is negligible.

We have found that it is usually necessary to consume 8–10 ml. of blood to obtain positive reactions with the amidopyrine, benzidine, Gregersen, and guaiacum tests. 5 ml. of blood produced weakly positive amidopyrine, benzidine, and guaiacum reactions in only two out of seven subjects, and did not produce a positive Gregersen reaction. The results of the four tests were similar, although the Gregersen and guaiacum tests were the least sensitive, and were negative in two subjects after the consumption of 10 ml. of blood.

With the in-vitro tests on graded dilutions of blood the Gregersen test was the most sensitive, and then the amidopyrine, benzidine, and guaiacum tests in that order of sensitivity, with each of the three specimens of blood tested. An explanation of the difference in the sensitivity of the Gregersen test in vitro and on fæces may be that in this test the fæces are not emulsified and so the reagent does not come into such close contact with any blood in the fæces.

As is to be expected, the in-vitro tests were considerably more sensitive with normal blood than with blood deficient in hæmoglobin. Hæmorrhage into the intestine sufficient to produce positive occult-blood tests may be several times as great in severely anæmic patients as in patients with a normal hæmoglobin value. We noted, during the investigation of a young man with severe hypochromic anæmia, that when the hæmoglobin value was only 3·7 g. per 100 ml. the occult-blood tests on his fæces gave only slight reactions, and might easily have been considered to be of no significance ; but when the hæmoglobin value had risen to 11·8 g. per 100 ml. the occult-blood tests became strongly positive.

Medicinal iron did not give a positive result with the amidopyrine, benzidine, Gregersen, and guaiacum tests either in vitro or on the fæces. It is unnecessary, therefore, to withhold iron therapy during the investigation of cases of hypochromic anæmia for occult bleeding from the gastro-intestinal tract. The subjects in this investigation were allowed to brush their teeth ; and, in view of our observation that 5–10 ml. of blood has to be consumed to produce a positive reaction with the occult-blood tests, we believe that it is unnecessary to forbid brushing the teeth, which is an unpleasant restriction for patients who have not neglected their oral hygiene.

In conclusion, we have not confirmed the previous observations that the benzidine and guaiacum tests are too sensitive, and that without dietary preparation they produce a high proportion of false-positive reactions ; and we believe that, with the four tests which we have investigated, a positive result is an almost certain indication of hæmorrhage, although occasionally a false weakly positive reaction occurs. A negative result has not the same diagnostic significance as a positive result, and, particularly in anæmic patients, moderate hæmorrhage may be missed. In choosing which test to use, the sensitivity of the tests need not be considered, but in general practice the Gregersen test is the one of choice because of its convenience.

Summary

The effects of normal diet and medicinal iron on the amidopyrine, benzidine, Gregersen, and guaiacum tests have been investigated. Medicinal iron does not produce positive reactions. Normal diet, not including black-pudding or liver, produces from 4 to 8% of weakly positive reactions, but does not produce positive reactions in any of the four tests.

The sensitivity of the tests was compared on serial blood dilutions and on the fæces of healthy subjects who had ingested a measured quantity of blood. The sensitivity of the tests on fæces is very similar, but on graded dilutions of blood the Gregersen test proved much the most sensitive.

With the exception of black-puddings, liver, and kidneys, dietary restriction is unnecessary, and brushing of the teeth need not be forbidden before carrying out the tests. There is little difference in reliability between the tests; and a positive reaction, particularly if repeated, is most significant. The tests are not too sensitive, and the degree of hæmorrhage necessary to give a positive reaction is greater in anæmic patients than in patients with a normal hæmoglobin value.

We wish to thank the laboratory staff for their help with the occult-blood tests, and Dr. G. R. Ellis and Dr. R. M. Evans for allowing us to make the investigation in their patients.

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GENERALISED MYOKYMIA IN THYROTOXICOSIS

REPORT OF A CASE

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MYOKYMIA is a form of muscle twitching due to spontaneous impulses arising in peripheral motor nerve-fibres. The movements are coarse enough to be seen through the skin and slow enough to be followed by eye. They are quite different from the darting irregular twitches of fasciculation which are gone almost as soon as seen. When large sheets of muscle are affected, a continuous movement results, which is very striking and has been called undulating myokymia. When the disturbance is more severe, the muscle goes into cramp.

Myokymia occurs as a normal phenomenon in the orbiculares oculorum muscles, for example, and in the calves, particularly after unwonted exercise. It can be seen three minutes after an ischæmia-producing bandage round the arm has been released. It occurs also in chloride loss, uræmia, and tetany, though in these conditions it is more often noticed as cramp. It can be detected in many cases of long-standing pressure on nerve-roots and is common in disc lesions. In these cases the myokymia is of course limited to the distribution of the affected nerves and is generally accompanied by signs of denervation. Kny in 1888 first described two cases of generalised myokymia. Other reported cases have been reviewed (Bittorf 1910, Neumark 1920, de Vries 1937). Many of these lasted a few months and appeared to be caused by some mild infection or toxæmia. Sweating and erythema of the palms and soles were common. Cases of unknown ætiology, lasting many years, have been described, also commonly with excessive sweating. Denny-Brown and Foley (1948) described two cases of this type and for the first time investigated myokymia electromyographically.

Myokymia persists during spinal or high nerve-block, showing that the disturbance does not originate in the anterior-horn cells. It is stopped by curare and is not potentiated by neostigmine, showing that it arises proximal to the end-plate. Its frequent occurrence in spinal-root compression and the ease with which it is produced by a compression bandage high up the limb rather than low down suggest that the proximal part of the nerve-fibre is predominantly the seat of the disturbance. It may be inferred that humoral changes, such as chloride deficiency and uræmia, which cause myokymia also chiefly affect the proximal end of the fibre. The electromyographic picture is characteristic, showing the twitches as trains of 3–6 or more identical motor unit potentials occurring regularly at the rate of 1–5 per second. Further, a single stimulus to an affected nerve is converted into repetitive impulses, showing that accommodation is lowered. Excitability is also increased. Signs of denervation are not characteristic of myokymia but occur when the myokymia is caused by compression lesions.

Myokymia, then, is due to heightened excitability and lowered accommodation of the proximal part of a motor nerve. It is the site of action that is characteristic, not the nature of the stimulus, which in fact may be of many kinds. When the disturbance is mild, a single impulse is followed by myokymia. When the disturbance is more severe, the myokymia is spontaneous and continuous. When the disturbance is most severe, the muscle goes into cramp. Myokymia may be regarded as the motor equivalent of the tingling due to disturbance of a sensory nerve.

Case-report

A married woman of 58 was seen at St. Thomas's Hospital in January, 1952. Apart from a depression in 1946, she was well until 1949, when she was suddenly taken ill with headaches. From then on she never recovered her former health, her main symptoms being anorexia and feeling weak, depressed, and undecided, making her unable to do her work as a housewife. In addition she lost 2 st. in weight and sweated profusely. Nine months previously she had become prone to cramps in her legs and her muscles "jumped."

She had been investigated in 1950 at another hospital. No firm diagnosis had been made, but she had been given methylthiouracil 0·3 g. daily because her basal metabolic rate (B.M.R.) was found to be raised (+29% and +17%). Treatment had been stopped after some months because there was no improvement.

When first seen by us she was apathetic, quiet, and despondent. She weighed 6 st. 5 lb. Her pulse-rate was 110 at rest. Her skin was pale and cold, and she had to change her clothes frequently because of sweats. Her thyroid was slightly enlarged, but there were no eye signs of thyrotoxicosis. The most striking feature was the continual undulating movement observable in the muscles of her face, tongue, limbs, and trunk. It was violent enough in the forearms to move the fingers. The buttocks and abdominal wall were in a continual state of movement. The musculature showed clearly because the subcutaneous fat had gone, but there was no obvious wasting of the muscles or any weakness. No abnormal signs were detected in her other systems.

Investigations

Electromyography showed that the muscle twitchings consisted of trains of 2–6 potentials occurring regularly 1–4 times per second. The potentials of each burst were of the same shape (see figure) and had the size and distribution of normal motor unit potentials. This indicated repetitive

Electromyogram, recorded with concentric needle electrode from left biceps muscle, showing characteristic motor unit discharges.

discharges from single motor nerve-fibres. The accommodation to slowly rising galvanic currents was low, being overcome in the right ulnar nerve at 3·2 mA (the normal by this method being 15 mA or more). The rhythm and form of the potentials were not altered by spinal anæsthesia, brachial-plexus block, or the administration of a neostigmine analogue (20 mg. of 'Tensilon' intravenously), but were completely stopped by *d*-tubocurarine. This showed that they originated in the peripheral nerve-fibres. Curves normal in intensity and duration, and the absence of true fibrillation potentials, on electromyography showed that there was no lower-motor-neurone degeneration. Voluntary contraction was accompanied by normal motor unit potentials with full interference patterns on maximum effort.

Neither carbachol (0·125 mg. subcutaneously) nor calcium gluconate (10 ml. of 20% solution intravenously) had any effect on the twitches, but these increased three minutes after the arm had been released from a fifteen-minute compression cuff, and they persisted during sleep.

The serum-calcium level was 8·9 mg., the serum-potassium level 15 mg., and the blood-urea level 48 mg., per 100 ml. The renal efficiency was 104% of average normal function, the plasma-alkaline phosphatase 11 King-Armstrong units, and the alkali reserve 62·6 vols. CO_2%. The B.M.R. (+30% and +28%) and serum-creatine level (0·93 mg. per 100 ml.) were both raised; the B.M.R. fell to +9% with complete muscle relaxation under general anæsthesia.

Progress

The myokymia was the most notable of this patient's symptoms. At first it was thought that she had idiopathic benign myokymia, like the two patients described by Denny-Brown and Foley (1948). The diagnosis of thyrotoxicosis was rejected, because of her clinical appearance, the high B.M.R. and serum-creatine level being tentatively attributed to the increased activity of the muscles. Nevertheless, when in April, 1952, the B.M.R. was brought to normal by a daily dose of methylthiouracil 0·6 g. given as a therapeutic trial, her sweating and tachycardia stopped, she put on nearly 2 st. in weight (8 st. 3 lb.), and she declared herself better than she had ever been for three years. Subtotal thyroidectomy was performed in July, 1953.

Four months after the start of treatment the myokymia was obviously less. After twenty-two months it was visible only in the point of the chin, the right brachioradialis muscle, and the buttocks, and was slight.

Discussion

The disturbance of the muscles was typical of myokymia clinically, electromyographically, and in its reaction to drugs. It was presumably due to some humoral disturbance, since it was generalised and was almost abolished after persisting unchanged for more than a year. The diagnosis of thyrotoxicosis was eventually proved by therapeutic trial despite the first doubts. In this connection it may be noted that McEachern and Ross (1942) showed that the B.M.R. is not raised by the equally extensive movements of progressive muscular atrophy. It may be accepted that the myokymia was due to the thyrotoxicosis since it stopped when the thyrotoxicosis was cured.

Have other cases of thyrotoxic myokymia been described? There are numerous references to muscle twitching in the literature of thyrotoxic myopathy. Most of these appear to have been fasciculation, but six cases were very similar to ours (Ayer et al. 1934, one case; Morgan and Williams 1940, two cases; McEachern and Ross 1942, three cases). In all of them there was widespread coarse muscular twitching very obvious on the abdomen and buttocks and apt to move the fingers or even the limbs. Signs of thyrotoxicosis were often slight, and though the cases were sometimes first diagnosed as progressive muscular atrophy they cleared up when the thyrotoxicosis was treated. The chief difference between these cases and ours is that they had wasting and weakness.

It might further be asked whether any of the chronic idiopathic cases were really missed thyrotoxic myokymias. This diagnosis is suggested by the fact that excessive sweating is often mentioned and any thyrotoxicosis might well have been remarkably mild. Denny-Brown, however, has assured us that his two cases at least were not thyrotoxic.

Summary

Myokymia is an undulatory movement of muscles and is due to spontaneous discharges from the proximal end of a motor nerve-fibre.

A case due to thyrotoxicosis is described.

Six previously reported cases were possibly of the same ætiology.

Thyrotoxicosis can now be added to the list of states that cause myokymia, and myokymia should be recognised as one of the rare phenomena of masked thyrotoxicosis.

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Preliminary Communications

OBSERVATIONS ON THE CAUSE OF DEATH IN EXPERIMENTAL ANTHRAX

UNTIL now there has been no evidence that *Bacillus anthracis* produced a toxin which might account for the cause of death in anthrax. Tissue-damaging factors had long been known to occur in extracts of anthrax lesions,[1] and recently Evans and Shoesmith [2] briefly described a rapidly occurring skin reaction produced by concentrates of old cultures of *B. anthracis*. However, they did not describe the specificity of this reaction or state whether the preparation was lethal. Its relation to the cause of death in anthrax, therefore, has yet to be established. More recently [3] we have suggested that guineapigs infected with *B. anthracis* die in secondary shock. This new hypothesis on the cause of death in anthrax [4 5] led to the demonstration of a specific, œdema-producing, lethal factor in the plasma of guineapigs dying of anthrax. Further chemical, histological, and clinical studies on such animals have strengthened the hypothesis. A summary of this work is now presented, together with observations on the loss of alkaline phosphatase from the infected kidney, and on a connection between the lethal factor and a protective antigen of *B. anthracis*.

SECONDARY SHOCK [6] AS A MAJOR FACTOR IN THE DEATH OF GUINEAPIGS FROM ANTHRAX

In the experimental infection used, guineapigs (700 g.) were infected intradermally with a dose of spores (strain N.P.) which killed all the animals within $3^1/_2$ days. In the 12 hours preceding death, the number of organisms in the blood rose from approximately $0{\cdot}3\times10^6$ to $1{\cdot}0\times10^9$ chains per ml. For a few hours following the initial invasion of the blood-stream, injection of streptomycin saved the lives of the animals, but if the bacteræmia had advanced beyond a critical point (ca. 3×10^6 chains per ml.) the abrupt ending of the infection with streptomycin failed to save the animals. They died 1–3 days later, although free from active infection. Hence the fate of the guineapig was not sealed until this critical point was reached, which was about 8 hours

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before death otherwise ensued. For this reason, the present study was confined to the final 10 hours of the disease when the major physiological changes occur.

The following observations are grouped under headings associated with shock. They are based on results with groups of 5–20 infected animals compared with a similar number of control animals. When the time of sampling is not given, the figures refer to infected guineapigs within about $1^1/_2$ hours before death. In the analysis of whole blood, corrections were made for the bacteria present.[7] Samples of plasma for analysis were filtered through 'Millipore' filters,[7] which did not alter the composition of normal plasma. Details of experimental methods will be reported later. They gave results with control animals which were within the normal range for each analysis.

(1) *Reduced Blood-pressure.*—Direct cannulation of the carotid artery under local anæsthesia showed the blood-pressure to be 84, 56, 39, and 10% of the normal value at approximately 9, 6, $1^1/_2$, and less than $^1/_2$ hour from death respectively.

(2) *Reduced Bleeding Volume.*—The maximum amount of blood obtainable by cardiac puncture was 33% of that obtainable from normal control animals.

(3) *Reduced Blood Volume.*—Estimates of the blood volume by means of red corpuscles labelled with radioactive phosphorus indicated a 25–40% reduction of the circulating blood volume.

(4) *Hæmoconcentration.*—Hæmatocrit, hæmoglobin, and blood-nitrogen determinations showed a 10–20% hæmoconcentration.

(5) *Presence of Œdema and Hæmorrhage.*—Plasma-protein nitrogen showed a 30% reduction. Much œdema and hæmorrhage occurs in guineapigs, as in other species infected with anthrax.[8]

(6) *Fall in Body-temperature.*—Rectal temperatures dropped from 99° to 88°F in the last 6 hours of classical anthrax, and from 90° to 80°F in the last 10 hours of those animals which were treated with streptomycin just after the critical point, and which died freefrom active infection 1–3 days later.

(7) *Rise in Plasma Inorganic Phosphate.*—This increased two and a half fold and the whole blood organic phosphates rose 13%.

(8) *Disturbance in Electrolyte Balance.*—The pH of the plasma was low, and there was a reduction in its Na^+. HCO^-_3, (40%), and Cl^- (7%) and a rise in its K^+, Mg^{++} (150%), and Ca^{++} (70%).

(9) *Interference with Carbohydrate Metabolism.*—There is a rise of 20% in the plasma-glucose in the early part of the final bacteræmia and a reduction of 20% in animals about $1^1/_2$ hours before death. This confirms previous work,[4 5] which showed an interference in carbohydrate metabolism in anthrax.

(10) *Evidence of Acute Renal Failure.*—Approximately $1^1/_2$ hours before death from classical anthrax, guineapigs had plasma non-protein-nitrogen and urea values of 92 (S.D.10) and 115 (S.D.12) mg. per 100 ml. respectively. This indication of renal damage was more pronounced in animals which were treated with streptomycin just after the critical point, and which died 2 days later free from active infection. In these animals anuria developed. Daily urine (5 ml. per animal) was low during the 2 days before death, even if a daily injection of saline (30 ml.) was given. Control animals produced 30 ml. of urine daily. Plasma non-protein-nitrogen and urea values for the dying animals were 185 (S.D.15) and 284 (S.D.43) mg. per 100 ml. respectively. Histological examination of the kidneys of these animals showed the tubular damage described below.

LOSS OF ALKALINE PHOSPHATASE FROM THE KIDNEYS OF GUINEAPIGS DYING OF ANTHRAX

Alkaline phosphatase determinations[9 10] on the plasma of guineapigs sampled approximately $1^1/_2$ hours from death gave a value of 191 (S.D.40) units per 100 ml., the normal value being 6·3 (S.D.2·4) units per 100 ml. This exceptionally high value merited further investigation.

The liver was not apparently the source of the enzyme, for there was no evidence of obstructive jaundice, or of gross histological damage, and tests on the plasma for bilirubin, thymol turbidity, and gold number showed no abnormality. No significant amount of alkaline phosphatase could be detected in extracts of *B. anthracis* grown in vivo, or in in-vitro-grown culture filtrates. However, the high concentration found in the urine of infected guineapigs (1760 (S.D.470) units per 100 ml.), compared to negligible values in normal urine, suggested the kidney might be a source of the enzyme, and this was confirmed by histological examination.

HISTOLOGICAL CHANGES IN THE KIDNEYS OF GUINEAPIGS DYING OF ANTHRAX

The kidneys show tubular damage that characterises a large group of conditions to which the term lower nephron nephrosis was applied by Lucké.[11] The term acute tubular necrosis or selective tubular necrosis is more descriptive. A full description is given by Hadfield[12] in a recent review. In addition to these tubular changes, summarised below, there are scattered areas where thrombosis in the smaller vessels is associated with large accumulations of bacilli. In these areas, groups of glomeruli may be found empty of blood. Changes in the tubules affect the proximal part of the nephron especially the descending part of the loop of Henle in the cortico-medullary region. Cloudy swelling is general and in places there is a definite cell necrosis with catarrhal desquamative change. Many nuclei are undergoing karyolysis and loss of desoxyribonucleic acid is demonstrable. The convoluted portion of the proximal tubules in the cortex show a swollen epithelium with some granular alteration in the mitochondria. Cell fragments with mitochondrial granules are present in the debris in the lumen.

Casts are present in the thin part of Henle's loop in the medulla and in some of the second convoluted tubules. These casts stain pink in eosin preparations. In some cases casts were present in the collecting tubules in the papillæ. In one case similar material lay free in the pelvis of the kidney.

Material from the kidneys of normal guineapigs and from five animals dying from anthrax was fixed in chilled formol saline for 12 hours. Preparations stained by Gomori's method[13] showed the distribution of alkaline phosphatase clearly in the normal animals. In the anthrax material it was found that there was an over-all reduction in the amount of alkaline phosphatase. There was patchy loss from the cortex of the kidney of one guineapig, and in the remaining four almost complete loss from the tubules of the outer cortex and a considerable reduction in the cells of the descending loop of Henle in the deeper layers. The casts seen in eosin preparations gave a positive reaction. A similar loss of alkaline phosphatase has been described by McManus in traumatic anuria.[14 15] It occurs in kidn ys of dogs in shock produced by the toxin of *Clostridium perfringens*[16 17] and also in alloxan[18] shock in dogs.

A CONNECTION BETWEEN THE SPECIFIC LETHAL FACTOR AND THE PROTECTIVE ANTIGEN OF *B. anthracis*

The demonstration of a specific lethal factor in the plasma of guineapigs dying of anthrax[2] immediately

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posed the question of its relation to a now well-established protective antigen [19 20] and to the capsular substance of *B. anthracis*.

The following evidence shows that there is a connection between the lethal factor and this protective antigen.

(1) Whereas the lethal factor kills mice and guineapigs and forms a large œdematous lesion in the skin of the guineapig, the protective antigen produced in vitro by Belton and Strange is completely non-lethal and produces no skin reaction.[21] Thus, 4 rabbits were unharmed by the intravenous injection of 50 ml. of antigenic filtrate prepared by our colleague F. C. Belton from cultures of the N.P. and Sterne strains. Even when tenfold ultraconcentrates of these filtrates were prepared, they proved harmless to mice (1 ml. intravenously) and provoked no reaction in guineapigs (0·2 ml. intradermally).

(2) Hyperimmune serum prepared in the horse [21] against the protective antigen obtained from in-vitro-grown cultures of a non-capsulated, avirulent strain of *B. anthracis* completely neutralised both the production of œdema by toxic guineapig plasma, and its killing power. In three tests, successive batches of toxic plasma (0·2 ml.) produced their œdematous skin reaction when mixed with normal horse-serum (0·1 ml.), but not when mixed with the antiserum (0·1 ml.) described above. In two tests the intravenous injection of mice with 1·0 and 0·5 ml. doses of toxic plasma killed respectively 10/10 and 10/15 animals. The same amounts of toxic plasma when mixed with half a volume of normal horse-serum killed 10/10 and 11/15 mice respectively. No mice died, however, when the antiserum to the protective antigen was used in place of the normal serum. Adequate batches of animals were used as controls.

(3) Plasma from guineapigs dying of anthrax was fractionated in the same way as that described for plasma/exudate.[22] The fraction (2% barium acetate/10% ethanol) which contained practically all the aggressin and protective activity, also contained tissue-damaging activity. In five fractionations of different batches there was a loss in the intensity of the skin reaction given by this fraction compared with that of the original plasma, but the other fractions were completely inactive.

On the other hand, the lethal factor does not appear to be connected either with the capsule of the organism or with polyglutamic acid. Firstly, the anthrax antiserum described above and that previously shown to neutralise the lethal factor [3] were derived from the Sterne uncapsulated strain of *B. anthracis*. Secondly, pure polyglutamic acid (34 and 80 mg.) produced by *B. anthracis* in vivo [22] and a fraction of toxic guineapig plasma containing 50–60% of this material [22] were non-lethal for guineapigs (250 g.) and mice respectively. No skin reaction was shown by either preparation.

A possible explanation of these results is that the protective antigen is a "toxoid" form of the specific lethal factor. The toxic properties of the latter are known to be unstable. It is destroyed completely when heated at 60°C for half an hour and is largely inactivated at pH 10 or 5, and during the fractionation described above.

These observations have been made solely with one strain (N.P) of *B. anthracis* in the guineapig. It is hoped to extend the work to test other strains and animal species.

Our thanks are due to Prof. E. J. King for confirming the analysis of alkaline phosphatase. Acknowledgment is made to the Chief Scientist, Ministry of Supply, for permission to publish this communication.

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THE USE OF THE RADIOACTIVE ISOTOPE OF COBALT Co^{58} FOR THE PREPARATION OF LABELLED VITAMIN B_{12}

THE use of vitamin B_{12} labelled with Co^{60}, for the study of B_{12} absorption from the intestine, was first described by Heinle et al.[1] Co^{60} is particularly useful for this type of work, since it emits a hard gamma radiation which is easily detected. However, because of the long half-life of this isotope (five years), and the unknown, but probable long, biological half-life of cobalt in man, the total amount which may be used with safety in any one individual is small. The Medical Research Council's Radioisotopes Panel has set the upper limit at one microcurie of Co^{60}. The amount of B_{12} labelled with Co^{60} which may be used in any one person is therefore limited, and this restricts the studies that can be made with this material. In order to increase the margin of safety, and to enable large or multiple doses to be given for the study of B_{12} metabolism, some other method of labelling the molecule is necessary. From the biological viewpoint the isotope Co^{58} is almost ideal for this purpose. Like Co^{60}, it has a hard gamma radiation, but unlike Co^{60} it has a relatively short half-life of seventy-two days, and may therefore be used in larger amounts. The only disadvantage of this material is the present difficulty in obtaining supplies.

We obtained Co^{58}, together with a small amount of Co^{60}, by irradiation of nickel, free from natural cobalt, in the Harwell pile. The reactions involved are Ni^{58} (n,p) Co^{58} and Ni^{60} (n,p) Co^{60}. The cobalt, when extracted, was added to culture medium and converted to vitamin B_{12} by a method previously described.[2] The product was purified by chromatography [3] on filter paper and then crystallised. The material so obtained had an original specific activity of 0·57 microcuries per microgramme of B_{12}. Of this radioactivity 90% was due to Co^{58} and 10% to Co^{60}, as determined by differential beta counting.

This labelled B_{12} has been used in parallel with Co^{60}-labelled material, in fæcal excretion studies. A dose containing 0·6 µg. of B_{12} was used in every case, the radioactivity of each dose being measured before being given. The dose was given to a fasting patient in the early morning, and nothing else allowed orally, for two hours. All stools passed were collected until less than 1% of the radioactivity was present in two consecutive stools. The stools were placed in a standard container and the radioactivity measured in a ring counter with eight Geiger tubes in parallel. Due allowance was made for the gradual decay of the Co^{58}. The following are some of the results obtained in a subject with pernicious anæmia in remission :

Method of administration	Percentage of administered dose excreted	
	Co^{60}-labelled B_{12}	Co^{58}-labelled B_{12}
With water only	100	95
With 20 ml. of pooled gastric juice	70	73
With a preparation of intrinsic factor	28	33

As was to be expected, the results with the two materials are, within the limits of experimental error, identical.

Because of the advantages of this material—namely, increased safety and the possibility of using larger

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amounts—we believe that, as supplies of Co^{58} become more freely available, the vitamin labelled with this isotope should replace that labelled with Co^{60} in clinical investigation.

Further studies with this material are in progress and will be reported later.

Our thanks are due to the Lederle Laboratories Inc., New York, for the supply of intrinsic factor preparation.

One of us (S. J. B.) was in receipt of a grant from the Nuffield Foundation, and wishes to acknowledge his gratitude.

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POTASSIUM DEFICIENCY IN THE PATHOGENESIS OF NUTRITIONAL ŒDEMA IN INFANTS

SODIUM, potassium, chloride, and nitrogen balance studies have been carried out on six infants admitted to hospital with nutritional œdema associated with incorrect post-weaning feeding and diarrhœa. Some of these cases conform to the description of kwashiorkor. All were admitted with hypo-albuminæmia and were treated with skimmed-milk formulæ. The findings are:

1. A considerable retention of potassium and nitrogen from the onset of feeding. The retention of potassium exceeds the theoretical potassium/nitrogen ratio of 3/1, being of the order of 9/1 for the first 3 or 4 days. Thereafter the rates remain constant at a figure of approximately 3·5/1 up to a period of 14 days—the longest balance period from time of admission.

2. There is an initial small retention for 2–3 days of sodium and chloride and a gain in weight. This is followed by a considerable negative balance accompanied by diuresis, loss of weight, and loss of œdema.

3. In two cases a mixture of sodium and potassium salts with glucose and water was given as the sole intake for periods of 4 and 5 days before milk was introduced. In both instances potassium was retained and a negative balance of water, sodium, and chloride, with modification of the œdema, was achieved while on this mixture. There was no change in serum-protein levels during this period.

4. Serum-potassium levels were significantly lower than normal on admission and rose with treatment. Serum-sodium levels could not be correlated with degree of œdema or treatment.

These data suggest that electrolyte imbalance is important in the pathogenesis of nutritional œdema of this type. Correction of potassium depletion can modify the œdema without correction of nitrogen depletion or alteration of serum-protein levels. There is evidence of reciprocal relation between potassium and sodium in this œdema. It is of interest in this connection that Black and Milne[1] showed that experimental potassium depletion causes sodium and chloride retention in man.

Further details of these studies will be published.

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Reviews of Books

William Clift

JESSIE DOBSON, B.A., M.SC., recorder of the Museum, Royal College of Surgeons of England. London: Heinemann Medical Books. 1954. Pp. 144. 21*s*.

THIS is the biography of the first conservator of the Hunterian Museum of the Royal College of Surgeons. Born of poor parents at Bodmin in Cornwall and compelled to leave school at the age of 11, he rose from the humble post of anatomical assistant to John Hunter to become a fellow of the Royal Society. Self-educated, he became an authority on his anatomical specimens and their use as an instrument of education. He was the man who cared for the museum during the years between his master's death and its purchase by the Government and presentation to the college: had it not been for William Clift, John Hunter's great work would never have been made available for future generations. He was responsible for its improvement and extension, but always within the pattern devised by his master.

The book is also a history of the museum and of the Royal College at one of its most exciting periods. The first president, Sir Everard Home, was a trustee under John Hunter's will. He retained Hunter's manuscript notes, systematically used them for his own writings, and finally burnt them so that the enormity of his offence should never be discovered. He died a chronic alcoholic, or, as one of the "intercepted letters" which we published in the last century, frankly put it, "always partial to the bottle, he became at last a regular sot and never went to bed sober." (*Lancet*, 1836–37, i, 646.) There are other extracts from *The Lancet* dealing with the annual Hunterian orations, which readers who have no knowledge of the feud between the Editor and the corporate bodies will find entertaining. Indeed, the whole book, though a little lengthy, is good reading. It is well illustrated, mainly from the drawings made by Clift and his son. When Clift died John Abernethy wrote of him as a man "on whose countenance benevolence had impressed a life-long smile; he who used to tell us, as boys, so much of all he knew, and to remind us, as men, how much we were in danger of forgetting, is now no more. How kind and communicative he was, how modest, and yet how full of information."

The effect of A.C.T.H. and Cortisone upon Infection and Resistance

Symposium held at the New York Academy of Medicine, March 27 and 28, 1952. Editor: GREGORY SHWARTZMAN, M.D. New York: Columbia University Press. London: Oxford University Press. 1953. Pp. 204. 45*s*.

THE changes which cortisone induces in the body's response to infection are occasionally brought home forcibly to the physician whose hormone-treated patient, while showing none of the classical signs of infection, nevertheless yields a blood-culture teeming with pathogenic organisms. Such an event dramatically emphasises the profound physiological and metabolic alterations which adrenal hormones may bring about in cellular and tissue responses to injury, stress, and infection.

In his introduction to this account of a New York Academy of Sciences symposium on these responses in relation to infection and resistance, Dr. Shwartzman points out that the isolation and physiological identification of adrenocortical and corticotrophic hormones have enabled experimental work on host responses to proceed in a fast-widening field. He himself is co-author of a chapter on experimental poliomyelitis which indicates how important the rôle of the host, apart from his immunity, may be in the pathogenesis of this disease. The other 29 contributors cover much ground, including the effect of corticosteroids on lymphoid tissue, on immunity and hypersensitivity, and on experimental specific infections. They are in general agreement on the potentiating effect on infection, although each piece of work inevitably gives rise to numerous hypotheses which demand further investigation. The chapter by Dr. Kabat and his co-workers is typical of the experiences of the cortisone-experimenter in this field. Investigating the effect of cortisone on acute disseminating encephalomyelitis in rhesus monkeys, they found that its immediate effect was to activate a spontaneous latent trypanosomiasis causing widespread lesions.

This book is an absorbing sample of contemporary work in America on host responses. It is often said that cortisone and corticotrophin are primarily research tools; it is clear that here they are in hands which exploit them with acumen.

Ergebnisse der gesamten Tuberkuloseforschung

Vols. 11 and 12. Editors: H. BEITZKE (Graz), S. ENGEL (London), L. HEILMEYER (Freiburg), J. HEIN (Tönsheide), E. UEHLINGER (Zürich). Stuttgart: Thieme. Vol. 11, 1953. Pp. 528. DM. 66. Vol 12, 1954. Pp. 488. DM. 65.

THE 11th volume of *Die Ergebnisse*, being the results of collective research in tuberculosis compiled by several authors under a joint editorship, includes such subjects as the pathological anatomy of the primary infection, and the extrapulmonary primary complex; avian infection in man; diabetes and tuberculosis; diagnosis and treatment of infection in childhood; and the place of such "stimulants" as smoking and alcohol in management—in which the author has taken up a middle, and rather lenient, course. Volume 12 records the death of Dr. Herman Beitzke in June, 1953. Much of the first part is concerned with articles on the anatomy and clinical manifestations of the tracheobronchial glands and atelectasis of the lung in tuberculosis, to which Dr. Beitzke had contributed. Wetzel discusses the various forms of tuberculosis of the spleen and reports 14 cases. Schäfer's article on tuberculosis and the organs of internal secretion is highly compact with an unrivalled bibliography. These volumes, like their predecessors, reflect much patience, industry, and learning. Besides being beautifully produced they are well illustrated, recalling the high standard of pre-war German reference works.

Diseases of the Knee

Management in medicine and surgery. ANTHONY F. DE PALMA, M.D., James Edward professor of orthopædic Surgery, Jefferson Medical College, Philadelphia. Philadelphia and London: J. B. Lippincott. 1954. Pp. 840. £8.

THIS is no mere compendium of the writings and experience of others, though the author makes full use of them and pays tribute where it is due; rather it is the fruit of very extensive experience, and the ability to learn from it.

The style is good and readable, and each section is complete in itself. On controversial issues, Dr. De Palma gives a fair-minded summary of current theories and opinion, but is not afraid to state his own choice. Though British surgeons may differ from him on some points they will commend his restraint; more than once, for instance, he makes a strong plea for the retention of the patella, which he regards as highly important to the function of the knee, and far from being an unessential sesamoid. There are very few omissions or errors (though we may not all agree that lesions of the fatpad are as uncommon as he believes, or that prominence of a cystic meniscus is at its greatest in full extension). The illustrations are profuse and the drawings outstanding, but the reproductions of radiographs are not always satisfactory.

For many years this will be a standard reference book on the subject, and one which any orthopædic surgeon would rightly be proud to have written.

Collected Works of C. G. Jung

Editors: Sir HERBERT READ; MICHAEL FORDHAM, M.D., M.R.C.P.; GERHARD ADLER, PH.D. Vol. 16. *The Practice of Psychotherapy.* Translated by R. F. C. HULL. London: Routledge & Kegan Paul. 1954. Pp. 368. 30*s*.

THE articles assembled in this volume have been written over a period of thirty years—from 1921 when the paper on the therapeutic value of abreaction appeared in its original form, to 1951 when Professor Jung put forward a temperate note on some fundamental questions of psychotherapy. In spite of the title, the articles do not deal with the technique of psychological treatment but with general problems. On these Jung states his opinion with modest firmness. Some of his dicta deserve wide attention. Thus he asserts roundly that "the art of psychotherapy requires that the therapist be in possession of avowable, credible and defensible convictions which have proved their viability either by having resolved any neurotic dissociation of his own or by preventing them from arising. A therapist with a neurosis is a contradiction in terms." In this, as in so many matters, Jung's view is opposed to that of the psycho-analysts: much of the earlier part of the book is devoted to explanation of the differences between individual psychology and its parent. The second part—"Specific Problems of Psychotherapy"—is mainly taken up with a study of the psychology of the transference, strangely based on the illustrations to a 16th-century alchemical work, the *Rosarium Philosophorum*. Dr. Jung rightly points out that unless the reader is acquainted with his book on *Psychology and Alchemy*, this exposition will be very hard going for him. It is, however, at once learned and illuminating, and it shows what a long and widening road Dr. Jung has travelled since he wrote his dissertation fifty years ago on the psychology and pathology of "so-called occult phenomena." Difficult as this concluding section may be for the uninformed reader, the book as a whole provides a mature and lucid statement of the place psychotherapy occupies in the *Weltanschauung* of a modern sage.

Dreams and Nightmares

J. A. HADFIELD, M.A., M.B. Harmondsworth: Penguin Books. 1954. Pp. 244. 2*s*. 6*d*.

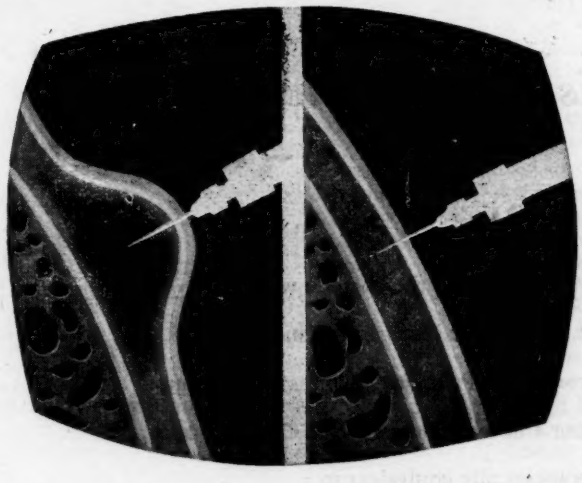
THE interest shown by all mankind from primitive savage to modern philosopher in the dream makes this examination of previous theories and of Dr. Hadfield's own hypotheses certain of a wide appeal.

He finds Freud's view of the dream as a wish-fulfilment unsatisfactory and incomplete, and is more sympathetic to Jung's belief that dreams represent an attempt by the dreamer's mind to deal with current life-problems. In Hadfield's opinion dreams are biologically determined, and by reproducing the unsolved problems of the dreamer are striving towards a solution. He gives many vivid and illuminating examples of dreams concerned with typical everyday problems. Writing on the nightmare, he ascribes the sensations of suffocation and nausea often accompanying this form of dream to autonomic disturbances produced in the dreamer by emotional or sexual conflicts, which are projected and experienced as external objects. The book concludes with two chapters on the relation of dreams to neurosis, and to psychical research.

Like all the author's works, this is well written and full of stimulating ideas.

Nash's Surgical Physiology (2nd ed. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1953. Pp. 686. 90*s*.).—The late Dr. Joseph Nash wrote his textbook of surgical physiology for the postgraduate student, the practising surgeon, the student, and the intern, in order "to present to them simply and briefly those aspects of physiology which are of especial importance to the surgeon." The need for six printings of the first edition shows that he achieved his object. Prof. Brian Blades, with the help of a team of eleven surgical teachers of the George Washington University, has revised the book, producing a useful, well-written, and up-to-date account of those aspects of physiology which bear on surgical problems. The practising surgeon will find helpful accounts of the things with which it is particularly difficult to keep up to date—shock, the physiology of burns, liver function, the behaviour of body-fluids, the endocrine glands, and the autonomic nervous system; and even if he occasionally gets lost—for example, amid the steroid chemistry of the adrenals—he will nevertheless find most of the book comprehensible and informative.

The Practice of Refraction (6th ed. London: J. & A. Churchill. 1954. Pp. 335. 21*s*.).—There have been no revolutionary changes in the practice of refraction, Sir Stewart Duke-Elder notes in his preface, since the last edition of this book. He has therefore had to confine himself to a few minor alterations and some additions—notably about contact lenses, which now have a chapter to themselves. Disappointing as this must be for him, it will matter very little to his readers: this was always a good book, and it still is.



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THE LANCET
LONDON: SATURDAY, SEPT. 4, 1954

Sickle-cells and Evolution

THE genes present, and their relative frequency, in any population will reflect its past social and medical experience. Genes and gene combinations which favour survival in the local circumstances of a long-established population will be relatively common there. Migrations into the area and racial mixture will tend to cause temporary disequilibrium with a tendency to return to the previous state of adaptation, perhaps in somewhat modified or improved form. Changes in the local environment will produce by natural selection alterations in gene frequencies tending to result in adaptation to the new circumstances. These processes are well illustrated by the fate of the gene responsible for the sickle-cell phenomenon.[1–3]

In 1910 Prof. JAMES HERRICK, of Chicago, found sickle-shaped red cells in the blood of an American Negro. In 1927 HAHN and GILLESPIE showed that this distortion of red cells took place only when the hæmoglobin was reduced, and that it could be demonstrated in the blood of about 9% of American Negroes. In 1944–46 several physicians—EVANS in West Africa, TROWELL in East Africa, ALTMANN in South Africa, and BEET in Northern Rhodesia—reported that sickle-cells were commonly present also in African Negroes. In many tribes the incidence was more than double that found in American Negroes. In 1949 PAULING and his colleagues showed that sickling was due to the presence of an abnormal hæmoglobin, which is now known as hæmoglobin S. Patients with severe sickle-cell anæmia have almost all their hæmoglobin in the S form, with the remainder as persistent fœtal hæmoglobin. Those with the sickle-cell trait—that is, with sickle-cells but without anæmia—have a mixture of normal adult and of S hæmoglobin. In 1950 PERUTZ and MITCHISON showed that hæmoglobin S in its reduced form had a low solubility, and that sickling was due to the precipitation of the hæmoglobin in ordered form. It is not yet certain how many of those with sickle-cell anæmia survive into adult life, but NEEL has calculated that in America the proportion is unlikely to be more than 25%. In America those with the sickle-cell trait are normally fit.

As early as 1923 HUCK had found that this trait was inherited as if due to a dominant gene, and the full genetical explanation of the sickle-cell findings was put forward in 1949 independently by NEEL and by BEET. They suggested that hæmoglobin S was determined by a gene allelomorphic to that responsible for normal adult hæmoglobin, the patients with severe anæmia and no adult hæmoglobin being homozygous for the abnormal gene, and those with mixed adult and S hæmoglobins being heterozygous for the gene. Investigation of apparent exceptions to this rule confirmed it by revealing that heterozygotes who were anæmic also had genes for other abnormal forms of hæmoglobin known as C or D, or the gene for thalassæmia, which does not give rise to an abnormal hæmoglobin but appears to inhibit the formation of adult hæmoglobin. More detailed examination of the frequency of the sickle-cell trait among various African tribes, notably by LEHMANN in Uganda, showed some surprising divergencies between one tribe and another. In general the Half-Hamitic tribes who live a pastoral life on the grass-lands, and also the Bantu tribes associated with them, showed little sickling. The Nilotic tribes and the Bantu, living in swamps and jungles, have an incidence of the sickle-cell trait of 20% or more; the highest incidence found was about 40%. Recently, too, the sickle-cell phenomenon has been found outside African and American Negroes. In 1950 LEHMANN, with prophetic insight, went to India and found a remarkably high incidence of the sickling phenomenon—over 30% in certain Indian tribes in the Nilgiri Hills of India. As in Uganda these tribes are culturally primitive forest-dwellers. Tribes living nearby with a pastoral culture were relatively free of sickle-cells. Since then the sickle-cell phenomenon has been found in Europe. CHOREMIS and his colleagues have reported an incidence of about 17% of the sickle-cell trait round Lake Copais in Greece; and SILVESTRONI and BIANCO have reported sickle-cells from Italy.

Sickle-cells thus pose a difficult problem in human evolution. How does a gene which is constantly being eliminated, by the death in early childhood of most of those homozygous for it, maintain a high frequency in some populations? Why does the incidence of the trait show such distinct geographical variation? One possible but improbable explanation is that in these particular parts of the world the mutation-rate to the gene responsible is high enough to balance the loss of the same genes from the death of most of the homozygotes. But this implies a quite extraordinarily high rate of mutation. Another explanation is that in the areas of very high incidence the homozygotes, because of gene modifiers, are only mildly affected, and only when this protection is lost by race crossing, as in America, is the disease severe. There is little information on the proportion of homozygotes that survive in Africa, but severe

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2. Allison, A. C. *Ann. hum. Gen.* 1954, **19**, 39.
3. Allison, A. C. *Trans. R. Soc. trop. Med. Hyg.* 1954, **48**, 312.

sickle-cell anæmia is being increasingly recognised there; and this explanation too is probably incorrect. Much the most convincing hypothesis is that by ALLISON, who has developed ideas first suggested by BEET. He notes that the frequency of the sickle-cell trait can be explained if the affected heterozygotes, in the areas concerned, are actually fitter than normals. BEET found that those with the sickle-cell trait relatively seldom had malaria parasites in their red cells. ALLISON confirmed this in a more homogeneous group, and found in a few Negro volunteers that normal persons were more easily infected with *Plasmodium falciparum* than were those with the sickle-cell trait. Secondly, in some areas with high incidence (above 10%) of the sickle-cell trait there is much infection with subtertian malaria. Some confirmation is provided by two of three reported series of affected children and adults. In these two series —one from Dar-es-Salaam and the other from Kampala—fewer of the children than of the adults had sickle-cells, as if a certain number of normals were selectively eliminated in childhood. The explanation of the relative immunity of those with some hæmoglobin S might depend on the fact that the *P. falciparum* is adapted to metabolise adult hæmoglobin and not hæmoglobin S, and that the presence of hæmoglobin S in the heterozygotes interferes with the parasite's metabolism of the adult hæmoglobin also present. Alternatively, the physical effects of the presence of hæmoglobin S might make the cell unsuitable for the parasite.

Several interesting deductions can be made from this hypothesis. First, the incidence of the sickle-cell trait must be applied cautiously in tracing racial affinities, particularly ancient affinities. The incidence of the trait might alter considerably in a few hundred years according to whether there was much subtertian malaria in the area. In an appendix to ALLISON's paper in the *Annals of Human Genetics* (as the *Annals of Eugenics* has been re-styled), SMITH [4] calculates the generations needed to produce by natural selection changes in the incidence of sickling in areas with much subtertian malaria, on the assumption that the fitness of the heterozygotes relative to normals in these areas is 1·26 (about the figure required to explain the present incidence). For a tribe with a low frequency of the phenomenon, such as that which would be produced by an average mutation-rate in the face of severe selection against the homozygote, it would take only some twenty generations to reach an incidence of 20%. Conversely, the eradication of malaria from these areas, which will abolish the selective advantage of the heterozygotes, will, unless the case-mortality of the anæmia is also reduced by some treatment, result in a steady fall in the proportion of heterozygotes and a more rapid fall in the proportion of children with severe anæmia. ALLISON suggests that such a reduction has occurred among Negroes in the U.S.A., the original slave immigrants being derived from populations of which probably more than 20% had the sickle-cell trait. This would have been reduced to something over 15% by cross-breeding with Whites and American Indians, but the further reduction to the present incidence of 9% he attributes to three hundred years' experience of a non-malarious climate. The spread of malaria control in Africa, then, may be expected to reduce gradually the number of children dying from sickle-cell anæmia. In areas where 40% of the population have the sickle-cell trait, possibly 40–50 one-year-old children per 1000 have this anæmia. Intelligent mating and family planning on the part of the parents with sickle-cell trait in these areas could bring about a very much more rapid reduction, without depending on natural selection by the death in early childhood of most of the homozygotes. Deaths from sickle-cell anæmia would stop altogether if the heterozygotes, easily picked out at a pre-marital examination, did not marry each other. This by itself would also stop all selection against the sickle-cell gene, and in time only about half the opposite sex would be available as spouses. But if in addition those with the sickle-cell trait planned a family size half that of normals, this would nearly halve the incidence of the sickle-cell trait in each successive generation, and in a few generations reduce the incidence to a level which would produce few cases of sickle-cell anæmia even if random mating were resumed. But clearly such a solution, depending on informed and willing coöperation, is not yet feasible.

It has long been known that in animals an individual heterozygous for a gene which causes a severe illness in the homozygotes may have greater fitness in certain circumstances than normals. If ALLISON's hypothesis is correct the sickle-cell phenomenon is the first example in man. Such a possibility should obviously be considered whenever a serious condition determined by a single gene in homozygous state is, in certain areas, commoner than would be expected from the conventional rates of gene mutation. Thalassæmia in certain Mediterranean countries, and perhaps fibrocystic disease of the pancreas in Great Britain and North America, may be further instances, since both are commoner than one would expect for conditions determined by a single gene.

Efficacy of Prophylactics

IN the earliest attempts to immunise against diphtheria it was found that passive protection conferred by the injection of antitoxin passed off rapidly. It was recognised that active immunisation with antigens produced by the bacteria was necessary for more permanent protection. At first, VON BEHRING [1] and PARK [2] used diphtheria toxin to which antitoxin had been added to diminish the toxic effects. An improvement was suggested by the work of HARTLEY,[3] who used toxin-antitoxin floccules, thus avoiding the injection of much foreign protein present in the crude culture filtrates and antitoxin. Meanwhile, RAMON [4] had shown that diphtheria toxin could be deprived of its toxicity, without destroying its immunising activity, by treatment with formalin; and GLENNY [5] and his associates found that addition of alum increased the potency of prophylactics. In the successful diphtheria immunisation campaign carried on in this country since 1940, alum-precipitated diphtheria

4. Smith, S. M. *Ann. hum. Gen.* 1954, **19**, 51.

1. von Behring, E. *Dtsch. med. Wschr.* 1913, **39**, 873.
2. Park, W. H. *Amer. J. Obstet. Gynec.* 1913, **68**, 1213.
3. Hartley, P. *Brit. J. exp. Path.* 1925, **6**, 112.
4. Ramon, G. *C.R. Acad. Sci., Paris*, 1923, **177**, 1338.
5. Glenny, A. T. *J. Path. Bact.* 1926, **29**, 731.

toxoid (A.P.T.) has been largely used. But, although A.P.T. is well tolerated by most young children, local or general reactions are fairly common in older persons or those previously immunised.

A number of reports [6–10] have suggested that patients with poliomyelitis are more likely to have paralysis in a limb which has been inoculated with mixed prophylactics containing aluminium adjuvants, especially in the presence of pertussis vaccine. Hence there is a tendency to return to the use of diphtheria toxoids to which no aluminium compounds have been added. It is therefore of particular interest to know what are the relative immunising efficiencies of prophylactics with and without aluminium adjuvants. Some information on this point is given in a recent report by BARR and CUNLIFFE.[11] In diphtheria injections it is important that circulating antitoxin should be available rapidly in the blood-stream to neutralise toxin before it causes tissue damage. But it was found that many student nurses entering hospital were Schick-positive and their blood contained little antitoxin, though many had been previously immunised against diphtheria. These nurses were reimmunised, one batch receiving purified diphtheria toxoid and the others A.P.T. Two weeks after the inoculation, and again twenty months later, the circulating antitoxin in the blood-stream was titrated. There was no difference in the immunising efficiency of the two prophylactics. Moderate or severe local reactions were produced, however, in a high proportion of those receiving A.P.T., but not in those immunised with purified toxoid. Excluded from the test were those nurses assumed to be hypersensitive, since they gave pseudoreactions with the Schick control fluid. It seems desirable therefore, in reimmunising young adults or older children, to avoid the use of prophylactics containing aluminium adjuvants and to test for hypersensitivity before giving boosting doses. This conclusion is reinforced by the result [12] of a large trial in 11 English county boroughs. Here an aluminium-phosphate-precipitated purified diphtheria toxoid (P.T.A.P.) [13] was used, and the conclusion was reached that this preparation has few advantages over other forms of alum-precipitated toxoid and that it is unsuitable for reimmunising children over 10, owing to the incidence of local reactions. In children who developed poliomyelitis within a month of the inoculation there was a significant association between the site of inoculation and the site of paralysis. It is satisfactory to note that out of 109,000 children given primary or reinforcing doses of diphtheria prophylactic during the four years of the trial only 1 child had diphtheria, and this child had in fact not received a reinforcing dose.

The problem of whooping-cough prophylactics is more complex for two main reasons: first, as the antigen responsible for eliciting the protective antibody is unknown,[14] a vaccine composed of entire bacterial cells is used; and, secondly, there are no simple tests that can be applied to the individual to detect immunity. Clinical trials can be conducted to test the efficacy of pertussis vaccines, but the results take so long to obtain that the vaccines tested are exhausted long before the test is completed. For the laboratory control of the potency of pertussis prophylactics, mice are immunised with the batch of vaccine, and they are then challenged by intracerebral infection with a living culture of *Hæmophilus pertussis*. Statistical examination of the results is necessary to evaluate the potency of the vaccine, and PITTMAN [15] suggests that a more accurate evaluation may be obtained by comparing the tested vaccine with a standard preparation, taking into account the number of bacterial cells present in the vaccine. Some commercial vaccines were found to be six times as effective as others. More careful standardisation would result in the elimination of ineffective vaccines on the one hand, and overdosage (with the increased risk of severe reactions) on the other. Mineral adjuvants, such as alum, were found to increase the efficacy of vaccines by some 70%, but the increased incidence of side-reactions has led to caution in this country in the use of vaccines containing aluminium adjuvants. We should perhaps add that many experienced immunologists nowadays recommend the use of the subcutaneous route rather than deep intramuscular injections for the administration of prophylactics, in order to minimise toxic side-reactions.

How Successful was the Operation?

THE country doctor usually has a fair idea of how much his patients have benefited from surgery: he sees them often, he knows when they are off work, and he is probably favoured with their relations' opinions. The busy general practitioner in a large town has less opportunity for direct observation of his patients and their lives; but if the results are really bad he will probably be told. Least likely, perhaps, to hear about the patient's condition is the surgeon who performed the operation; for even if he takes a great deal of trouble he may still not get the truth. We often hear about patients who exaggerate their symptoms—mildly when applying for a certificate of absence from work, and more severely when bringing an action for compensation. But we hear less of those who feel that the doctor has done his best and taken great pains, and if the end-result is not entirely satisfactory it is not for someone who has been described as "one of my best cases—I'm going to write to *The Lancet* about *you*" to let the medical side down. Thus the affable old porter who has had an operation for gastric carcinoma assures his surgeon some years later "haven't had a day's illness since, sir," though he is actually attending another hospital for pernicious anæmia. "Such a nice gentleman. I couldn't disappoint him."

How then should the follow-up be done? In her article on p. 485, Mrs. SHEPHERD offers a strong case for the independent assessor; but even this neutral observer (as she explains) meets some difficulties in eliciting the facts. There is the initial task of getting the patients to come to be assessed; and unless much care is taken over this the sample will not be

6. McCloskey, B. P. *Lancet*, 1950, i, 659.
7. Martin, J. K. *Arch. Dis. Childh.* 1950, **25**, 1.
8. Geffen, D. H. *Med. Offr*, 1950, **83**, 137.
9. Hill, A. B., Knowelden, J. *Brit. med. J.* 1950, ii, 1.
10. Korns, R. F., Albrecht, R. M., Locke, F. B. *Amer. J. publ. Hlth.* 1950, **42**, 153.
11. Barr, M., Cunliffe, A. C. *Mon. Bull. Minist. Hlth Lab. Serv.* 1954, **13**, 198.
12. *Ibid*, p. 127.
13. Holt, L. B. *Lancet*, 1947, i, 282.
14. Pillemer, L., Blum, L., Lepow, I. H. *Ibid*, 1954, i, 1257.
15. Pittman, M. *J. Pediat.* 1954, **45**, 57.

representative. In her survey the best results were obtained at a hospital where the surgeon sent a signed personal letter to each patient asking him to come, and offering expenses where necessary. This brought a response of 93% of those invited. Routine letters explaining, and asking the patient to attend, sent by the hospital, usually brought a response of over 75%. It is as well, she says, to offer fares; the sums required are seldom large, and they may make all the difference to the proportion of attendances. Patients left with any difficulty in walking may also need an offer of transport to bring them in. At interview the independent assessor—provided he or she inspires confidence—will probably learn more than the surgeon who did the operation. But patients are usually loyal, and they are more willing to talk if they are convinced that the assessor is there with the consent and good will of the surgeon. For this reason Mrs. SHEPHERD recommends that the interview should be arranged either to coincide with the surgeon's own clinic or as a routine follow-up visit. Moreover patients are likely to be more friendly and communicative if they are treated with consideration; and, since they are attending in the interests of science rather than in their own, they deserve a definite appointment and a cordial reception. They should have the assessor to themselves during their talk, for in a confidential atmosphere they are more disposed to offer candid comments on their experience. The assessor's examination should be thorough and carried out in the same manner with every patient, so that the results are comparable; and, needless to say, uniform record-cards should be used. As for the patients who fail to attend, a questionary sent by post will sometimes evoke a fair response from them, but the data thus obtained are less satisfactory. It is much better for the assessor to call on them, since "the patient's reactions to a question by an interested person, face to face, and one on a type-written or printed sheet are very different." People hesitate to set down and sign a criticism of what has been done for them, whereas a little tactful questioning will quickly elicit their disappointment.

There remains one aspect of assessment which Mrs. SHEPHERD does not mention: what contribution can be made by the general practitioner? He is, after all, a neutral observer who may have much information about the patient at his disposal; and some will think he should himself be the assessor of his own patients. The objections to this are statistical. If a surgeon performed arthroplasty on 30 patients, and if these were on the lists of 6 different general practitioners, there would be 6 different assessors of the series, and it could not be claimed that the results were comparable. Nevertheless it seems reasonable that the single assessor, in the hospital, should have access to the comments of the patient's own doctor, and that these should cover not only the time since the operation but the patient's condition before it, and include some estimate of his temperament and outlook—not always easy to evaluate correctly at a first encounter. Together patient, family doctor, and assessor—respectively providing candour, experience, and impartiality—can give the surgeon information which may be one of the most useful, if least visible, of his instruments.

Annotations

TOWN-DWELLER'S AIR

ONLY 18% of the coal consumed in Great Britain every year is burned on domestic hearths; yet these contribute 45% of the smoke in which most of us now spend our lives. They discharge over us annually 900,000 tons of smoke, 100,000 tons of grit, and 900,000 tons of sulphur dioxide; industry adds another 800,000 tons of smoke, 200,000 tons of grit, and 1,800,000 tons of sulphur dioxide; and there are further increments from electricity works, railways, coke ovens, and gas works. When an inversion develops, so that cold air lies still and stagnant under a layer of warm air, these poisonous or unpleasant things collect about us visibly, and—as happened in 1952—kill large numbers of us.

P.E.P. note [1] that smog destroys health as well as life. It quotes a Government committee of inquiry (the Newton Committee [2]), which more than thirty years ago held that the chronic pollution of the air may well be partly responsible for the higher incidence of bronchitis and other respiratory ailments in towns as compared with the countryside. The screening of sunlight by the smoke pall, too, is probably detrimental to health: the natural light of the most heavily polluted area of a city in winter may be less than half that of the outskirts. It is also possible, of course, that coal smoke is among the factors responsible for the higher incidence of lung cancer in towns—and the smokier towns especially—as compared with rural areas; indeed, in the ætiology of this disease, coal smoke and tobacco smoke may well reinforce each other.[3]

Nowadays, however, even the rural areas of this small island have their smoke pall: indeed some of our annual 7 million tons of pollution drift not only across the countryside but—in defiance of the Entente Cordiale—over to France. Though most of the heavier particles emitted tend to settle near their source, even our cleanest rural areas have deposits amounting to 3–4 tons per square mile per month. The towns have anything from 10 to 50 tons. In hazy or foggy weather concentrations of both smoke and sulphur dioxide increase: in the 1952 smog they were at least 14 times greater than usual, and are thought to have risen sometimes during the five days to 50 times the normal levels. The cost of smoke, in damage and destruction of materials and buildings, in cleaning, in loss to agriculture, in delays in transport, and in waste of combustible fuel has often been assessed, and was put last year, on a conservative estimate, at £150 million per annum.[4] To get rid of smoke could hardly cost much more, and once clean air was achieved we should begin to save some of this reckless outlay.

At present the law takes no account of domestic smoke, does not control in any way the factors which lead to smoke being made, and can only take effect when smoke has reached the standard of a nuisance. In short, the law has some feeble curative powers and no compulsory preventive powers at all. There have been, however, some useful local Acts; and in fact, as P.E.P. point out, a new phase of smoke-control legislation began with the Manchester Corporation Act of 1946. This introduced two new principles—the prior approval of all new fuel-burning plant, and the smokeless zone. We now have three smokeless zones—in Manchester, Coventry, and Rochdale—and others are soon to appear in the City of London,

1. *Planning*, 1954, **22**, no. 369. Published by Political and Economic Planning, 16, Queen Ann's Gate, London, S.W.1.
2. Interim report of the Government Departmental Committee on Smoke and Noxious Vapours Abatement. H.M. Stationery Office, 1920.
3. Stocks, P. *Smokeless Air*, Winter, 1952.
4. *Times*, April 20 and 21, 1953.

Bolton, Tottenham, and Salford. These are at present concerned mainly with industrial smoke, since they embrace areas where dwelling-houses are few; but some authorities—notably those of Bradford and Nottingham—are making it a condition of tenancy on their new housing estates that only smokeless fuel should be burned. New national legislation is badly needed, however; and should cover, P.E.P. suggests, better methods of controlling railway smoke, and means for dealing with the pollution problems of iron and steel manufacturers, coke ovens, and cement works. Research, too, is needed, possibly under the direction of a Government technical committee. Qualified inspectors, covering the whole country, are essential, to see that efficient methods are being used. At present of our 4600 sanitary inspectors only 423 hold a certificate in smoke inspection, and only 25 are working as specialist smoke inspectors. The open domestic grate, P.E.P. believe, should now be discarded in favour of appliances (such as the open-close stoves) which burn fuel completely and much more economically; and the public taste for smokeless fuel might be encouraged by increasing the price of raw bituminous coal (which costs the country so much in disease, dirt, and destruction) while keeping that of the smokeless fuels unchanged. Before discriminating between fuels in this way, however, the smokeless brands ought to be made available to all consumers who wish to buy them. At present there is not enough of them about. The National Smoke Abatement Society, to which P.E.P. pay great tribute, believe that the output of these fuels could be rapidly increased, and that the present annual consumption of 5 million tons in domestic grates could be raised to 10 million tons by 1957 and 15 million tons by 1962. This society, working on a shoestring, has done more than any other agency to educate the public in the dangers of air pollution. It is time to heed its warnings, and get on with the job.

BLOOD-VESSEL SUBSTITUTES

THE replacement of diseased sections of the larger blood-vessels by arterial homografts is now a practical surgical method. It is over six years since the first aortic graft was inserted in a case of coarctation of the aorta, by Gross, of Boston.[1] This graft is still functioning well. The success of the technique, now widely practised, has stimulated the search for an artificial blood-vessel substitute, particularly in America where it has proved difficult to obtain enough arterial homografts. At the meetings of the International Society of Angiology and of the American Society for Vascular Surgery in San Francisco in June this year, no less than four papers dealt with a more or less successful outcome of this quest.

The almost incredible fact is that in a large blood-vessel, such as the aorta, a tube fashioned from quite a large selection of the newer plastic materials will function as a substitute for a segment of the aorta. Tubes of 'Vinyon-N' (nylon) cloth were first used experimentally in Blakemore's unit in New York. A tube of the required diameter and length is made by folding the cloth over a glass rod of suitable size and hemstitching down one side. The ends are then folded back in a cuff to exactly the length required, and the cloth tube (carefully washed and cleaned and sterilised by autoclaving) is sewn into place, in exactly the same way as an arterial graft. Technical considerations are important—for instance, unless the tubes are sewn in under tension they tend to wrinkle and kink, which predisposes to thrombosis. Experimentally, where the technique has been satisfactory such tubes have remained patent for upwards of a year. Fibrous tissue grows into the interstices of the cloth, and the tube acquires an endothelial lining and in time looks remarkably like the original blood-vessel.

Hufnagel, of Washington, D.C., has had equally good results with 'Orlon' cloth. He has also shown[2] that segments of aorta can be successfully replaced by rigid tubes of methyl methacrylate ('Plexiglas'). The method of fixing the ends of these tubes to the ends of the aorta, by means of a toothed nylon ring, is extremely ingenious, although somewhat complicated and expensive. Such tubes, containing a special ball-valve to compensate for an incompetent aortic valve, have been inserted in the aorta of patients and have remained patent and perfectly satisfactory for about a year and a half so far.

Other plastic tubes which function fairly successfully have been developed by Shumaker of Indianapolis (vinyon cloth with 'Polythene' backing) and by Grindlay at the Mayo Clinic (tubes of 'Ivilon' sponge, which consists of a mass of fine polythene fibres).

All these vessel substitutes apparently work fairly well in large vessels such as the aorta. They are not so successful when applied to vessels of smaller calibre. In certain centres the experimental work has advanced far enough to warrant trial in man. Hufnagel, Blakemore, and Shumaker have all successfully replaced abdominal aortic aneurysms with cloth tubes, which seem to be functioning perfectly well to date. There are many difficulties and limitations to this technique, but it opens the door to fresh possibilities in vascular surgery.

EVENING COLIC

WITH the conquest of many of the serious diseases of infancy, more heed is being paid to minor troubles. Thus fresh thought has been given to such problems as circumcision[3] and umbilical hernia,[4] with the result that much unnecessary surgery has been eliminated. Professor Illingworth,[5] in Sheffield, has been investigating a common disorder of early infancy that has hitherto received less than its fair share of attention.

About a quarter of all infants in their first three months of life have screaming attacks in the evening. This disturbance has been termed "three-months' colic"—a designation that Illingworth accepts, though he acknowledges that it is unsatisfactory.[6] In the attacks, which keep on recurring for three or four hours, the baby draws up his legs, clenches his fists, goes red in the face, and emits piercing screams. The distracted mother is reassured by well-meaning neighbours that "he'll grow out of it," and so he does; but meanwhile she will usually have gained a few grey hairs. The father, too, may have his early relations with his child soured by these bouts; for, on his return home, the mother's assurance that the baby has been perfectly good all day suggests that it does not like him.

The screams are generally thought to be due to colicky abdominal pain, but the cause of this pain is far from clear. Illingworth gives a long list of factors that have been blamed: these include overfeeding and underfeeding; too rich feeds and too weak feeds; feeds given too hot and feeds given too cold; allergy to milk, cod-liver oil, or orange juice; faults in handling the baby (overstimulation, exposure to cold, abdominal binders); over-anxiety of the mother; and fatigue at the end of the day.

Illingworth undertook a controlled investigation of 50 babies with colic and 50 healthy babies. The results are not conclusive. The mother's age, parity, and course of pregnancy did not differ materially between the two

1. Gross, R. E. *J. Amer. med. Ass.* 1949, **139**, 285.
2. Hufnagel, C. A. *Bull. Georgetown Univ. med. Center*, 1951 **4**, 128.
3. Gairdner, D. *Brit. med. J.* 1949, ii, 1433.
4. Woods, G. E. *Arch. Dis. Childh.* 1953, **28**, 450.
5. Illingworth, R. S. *Ibid*, 1954, **29**, 165.
6. Illingworth, R. S. The Normal Child. London, 1953.

groups; and full assessment showed no significant difference between the colicky babies and the normal controls. Slightly more babies with colic were breast-fed, and their weekly gain in weight was slightly greater; but the differences were not significant. Underfeeding seemed most improbable in either group, since the weight gains were very steady and most of the babies were above the expected weight. Like most pædiatricians, Illingworth believes that overfeeding rarely, if ever, occurs in infancy; and certainly there was no evidence of it in this series.

The most likely cause of the colic is excessive wind in the bowel, or wind somehow trapped in a loop of bowel. Loud abdominal rumblings can usually be heard during the attacks, and relief often seems to coincide with the passage of flatus per anum. Jorup [7] has investigated the amount of gas in the bowel in babies with colic and found no clear evidence that it was excessive. Illingworth, who repeated these studies, agrees with Jorup's conclusion. It is, however, extremely difficult to assess the amount of gas from a straight abdominal radiograph, and, unless there is intestinal obstruction, even more difficult to be sure of its distribution in the bowel. Under the age of 18 months gas in the bowel is equally distributed between the small and large intestine.[8] A slightly increased quantity in the small intestine, insufficient to cause any alteration in the radiographic appearances, could conceivably cause an air-lock and produce colicky pain. Jorup gave barium enemas to infants with colic and found that the barium was usually forcibly expelled. The attacks of pain appeared to coincide with colonic contractions and were provoked by feeding, whether from breast or bottle, also by sucking on an unperforated teat. Mere contact with the mother without suckling did not cause colic. Jorup also measured the rectal pressure during feeding. He found that the normal pressure was less than 60 cm. H_2O with fluctuations of about 25 cm., whereas in infants with severe colic pressure was much higher with greater fluctuations. He suggests that parasympathetic predominance may explain these findings.

In treatment most of the suggested remedies have proved ineffective, but Jorup found that methylscopolamine nitrate always relieved the symptoms. A controlled investigation of the value of this drug is now proceeding in Sheffield.

PLEURITIC PAIN

THE referred pain of pleurisy is a valuable guide to the part affected. Thus apical pleuritic pain is felt along the inner side of the arm in the area supplied by the humeral branch of the 2nd intercostal nerve, whereas pleurisy of the lateral areas is felt along the intercostal nerves and in the muscles, sometimes fairly closely over the area involved. Basal or diaphragmatic pleurisy and apical pleurisy may give rise to referred pain at the same site. The sensory nerves of the central part of the diaphragm run in the phrenic nerve, which has an upper-cervical origin; and pain is referred to the neck and shoulder—often to some part of the trapezius muscle. But the apical part of the parietal pericardium is also supplied by the phrenic nerve and has the same site of reference. The outer part of the diaphragm is supplied from the lowest six intercostal nerves, and pain may be referred over an area extending from upper to lower abdomen and into the lumbar region.

Just how this referred pleural pain arises is uncertain. Originally it was believed to be caused by friction between two rough, inflamed surfaces. But, as Bray [9 10] has pointed out, this hypothesis is easily disproved by asking the patient to hold his breath at full inspiration, when there is no movement or friction and yet pain may be considerable. Furthermore, pain may persist even after the pleural surfaces have been widely separated by therapeutic pneumothorax.[10] This also rules out traction from adhesions as the cause of pain. Mackenzie [11] thought that the pain was due to spasm of intercostal muscles, since at operation for rib resection he found that the pleura was insensitive. Possibly he was right that muscles go into spasm over the site of a lesion in the thorax, just as in the abdomen; but he was wrong in thinking that no pleural surface was sensitive. Capps [12] has shown that parietal, but not visceral, pleura is highly sensitive. During thoracocentesis he inserted a silver wire into the thoracic cavity and touched several different sites. From his observations in patients and normal persons he found that he could mimic the referred pain of pleurisy, but only when the parietal pleura or diaphragm was touched. Bray [9 10] has put forward the tension hypothesis of pleuritic pain. The parietal pleura lines the inner wall of the thoracic cage and is stretched during inspiration; it is an elastic and well-lubricated membrane, and normally no sensation from it is perceptible. When the pleura is inflamed it becomes hyperæsthetic and stretching causes pain. This may be likened to the hyperæsthesia of an inflamed area of skin.

There are anatomical grounds for Bray's hypothesis. The sensory nerve-endings in the parietal pleura are of two kinds: (1) a network of free endings of non-medullated or poorly medullated fibres both with and without capsules, and (2) pacinian corpuscles.[13] It is said that some of the free nerve-ends lie actually in the cytoplasm.[14] From comparative observations on various parts of the body it seems clear that pain depends on the presence of the free nerve-ends. In the dermis these form a closely interlocking, but not syncytial, network [15]; and much the same is true of the parietal pleura. Pacinian corpuscles, with their overlapping leaves surrounding a bare nerve axon, are like a "system of levers working against an elastic restraint" [16] and are admirably adapted for response to mechanical deformation in any direction, either by compression or by stretch of the membrane in which they lie; they will fire off a stimulus in response to an 0·5 μ deformation applied in 100 μ second.[17] Thus the parietal pleura is supplied by both stretch and pain receptors, but in health they are not stimulated—or not to an extent which reaches consciousness. In some way they are sensitised by inflammation. Why response to a stimulus, particularly a painful one, is stronger or more apparent to the senses when it arises from a part whose blood-vessels are dilated is not known. From observations on the skin it has been found that a strong stimulus applied to a specific receptor calls forth only the sensation proper to that receptor. The pleura contains tension as well as pain receptors; yet the only sensation to which it ever gives rise is pain, and apparently stretch is the stimulus. Possibly when stretch receptors are activated they affect the free nerve-ends and cause a local—or perhaps a central—reinforcement. If this is not so, the function of the pacinian corpuscles is mysterious; it has never been suggested that these are concerned with the unconscious control of normal respiration.

On both anatomical and physiological grounds, there is good reason to accept Bray's tension hypothesis of pleuritic pain.

Dr. ALFRED COX, secretary of the British Medical Association from 1912 to 1932, died on Aug. 31 at the age of 88.

7. Jorup, S. *Acta pædiatr., Stockh.* 1952, **41**, suppl. 85.
8. Paine, J. R., Nessa, C. B. *Surgery*, 1942, **11**, 281.
9. Bray, H. A. *Amer. Rev. Tuberc.* 1926, **13**, 14
10. Bray, H. A. *Ibid*, 1954, **69**, 634.
11. Mackenzie, J. Symptoms and their Interpretation. London 1920.
12. Capps, J. A. *Proc. Ass. Res. nerv. Dis.* 1942, **23**, 263.
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Special Articles

INDEPENDENT ASSESSMENT OF RESULTS OF OPERATION

An Approach to Clinical Research

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IN 1950 the British Orthopædic Association decided to investigate the results of arthroplasty of the hip. The investigation was to be made at five different centres, and it was thought that a survey of this kind would be of most value if an independent reviewer was appointed to see the patients after operation.*

I was asked to be this clinical assessor, and an account of some of the lessons I learned in planning and carrying out the investigation may help others to avoid time-consuming mistakes.

COLLECTING THE PATIENTS

In reviewing a large series of cases there are three main considerations: (1) to obtain a statistically satisfactory number of patients for examination; (2) to elicit the maximum of information from them; and (3) to record the examination in a form suitable for assessment and comparison.

It is essential to know from the beginning which patients are to be included in the survey. A full list should be made from operation registers, or ward-admission books, or the files of the records department. The list must be in chronological order so as to show that there has been no selection of patients. Opening and closing dates should be fixed at the outset. The following headings should be included: Date of operation; name; address; likelihood of patient attending; remarks. If the number of patients who are unlikely to be able to attend is more than a certain proportion of the total, the figures obtained will be statistically insignificant. Only if the percentage of probable attenders is high enough can the investigation proceed.

I asked for lists at much too late a stage. At one hospital the surgeon suggested that, as patients returned for years to his follow-up clinic, enough material would be secured if the patients who attended each session were seen. This led to waste of time, and was soon abandoned. Not all surgeons realise the importance of a high-percentage follow-up. One patient who had already filled in his stamped addressed postcard to say he would attend, was told by the surgeon (who saw him a week earlier) that he need not do so. The secretary was asked to report that "he isn't a good result anyway." Another surgeon drew his patients from a wide area, and the list, when eventually obtained, showed so many patients against whose name was the remark "Not sent for, as lives too far away," as to invalidate, statistically, any conclusions.

ARRANGING FOR THEM TO COME

Exactly what percentage attendance can be considered satisfactory must vary with the type of case. In hip operations unsatisfactory results are associated with decreased mobility of the patient, who may be unwilling or unable to make the effort to attend. On the other hand, many patients with the most satisfactory results are back at work and cannot take time off. The pleased, usually grateful, patient makes every effort to attend—"It was the least I could do." But a surprising number of disgruntled patients also came. Their answers to the question: "Was the operation worth while?" varied from a plain "No" to an aggressive "That's what I'd like to know!" a wistful "I'm still hoping," and even one menacing "I wanted to see Mr. X to tell him just what I thought of this!" Some of these less happy patients come for the sake of having a fresh opinion.

To get the highest possible attendance a personal letter should be sent to each patient, signed by the surgeon himself, and offering expenses where necessary. By this method one surgeon in this review achieved an attendance of 93% of his hospital patients. Routine letters of explanation, with a request to attend the hospital for an examination usually produced an attendance of over 75%. Letters ought to be sent out two weeks before the date on which the patient is asked to attend. This allows time for other patients to be substituted for absentees.

Some hospitals had a fund from which patients could be paid if they were worried about expenses; other hospitals ignored the problem. In one the project had to be abandoned, because the surgeon was not prepared to ask patients to come for examination unless expenses were forthcoming. The amounts involved are not large, and attendance is undoubtedly encouraged by an offer to defray expenses. Transport was arranged from all hospitals where this was thought necessary. This is a legitimate charge on the National Health Service where the visit takes the place of a routine attendance at follow-up clinic.

It is usually inadvisable to see patients continuously in one centre. The extra work thrown on the secretarial and nursing staffs becomes a burden. Two days a week will probably provide as much extra clinical material as the radiological departments or the laboratory can manage. I found it convenient to visit two hospitals for two days on alternate weeks, thus allowing for each a fortnight's interval.

The reviewer, who is examining similar types of cases day after day, will find the work both trying and exacting. Fewer mistakes and omissions in detailed recording are likely to be made if a quiet consulting-room is available rather than a cubicle in a noisy out-patient department.

Secretarial help is important. The help I was offered varied from an efficient secretary from the records department, who arranged the attendances of the patients and then acted as receptionist, to the joint help of a private secretary, who wrote to the patients, and a sister in charge of a busy fracture clinic at the examination. It would have saved much time to have had a secretary of my own to help in the organisation, and where necessary to attend the clinical examinations. The cases for each day are best selected by a secretary at the hospital, who has local knowledge of places and people.

THE INTERVIEW

If possible the review should be arranged to coincide with the surgeon's own clinic; for the patient is, naturally, most satisfied, and therefore most coöperative, if he sees his own surgeon as well as a stranger. Almost equally good is an arrangement with the surgeon that the review visit may take the place of a routine follow-up visit. This arrangement shows the patient that there is an understanding between his surgeon and the reviewer.

To elicit as much reliable information as possible in a short time the patient's confidence must be quickly won. A patient is more ready to coöperate if he is shown consideration, and given a definite appointment. All details should be extracted from the case-sheets and earlier X-ray films before he arrives. Clinical records vary remarkably. In teaching hospitals notes may be full, but there are often discrepancies between records made in the outpatient department and those made after arrival in the ward perhaps only a few days later.

* A detailed report of the results of the clinical investigation will soon be published in the British volume of the *Journal of Bone and Joint Surgery*.

Sometimes clinically incompatible facts are recorded in the same notes. Often—and this applies particularly to private patients—the surgeon has made notes in general terms adequate for his own guidance, but lacking some of the figures and facts needed for a review. Supplementary information is best obtained from the patient at the beginning of the interview when his mind is fresh.

Uniformity in the examination is necessary—the patients undressing adequately and to the same extent, and the examiner using the same methods and apparatus throughout. For a hip examination, the anterior superior spines must be uncovered. Unless this is done it is impossible to measure a limb accurately or to differentiate pelvic tilt or rotation from hip movement. Almost all patients appreciate thoroughness in an examination.

The reviewer should see the patient alone. Patients are more guarded in what they say when a third person is present, and if the third person is their surgeon, they are anxious not to appear to criticise him or their treatment. On one occasion a surgeon demonstrated six cases to me. They were good results, and only one confessed to having any pain at all. Another six I asked to be allowed to see on my own. These were similarly good results, but only one said there was no pain.

FINISHING TOUCHES

Uniformity in recording is essential to permit later analysis and comparison. A proforma must therefore be used. A draft is used for ten or more patients and the findings recorded. With the main object of the review in mind, these proformas are critically scanned, and omissions and irrelevancies are corrected. A blank space should be left for extra information or illustrative sketch. As the proformas will be much handled, paper of good quality should be used. The symbols and abbreviations employed should be simple, and not liable to be confused. Reliability of the analyses depends on accurate interpretation of the records.

When satisfactory lists of patients have been drawn up, and the proforma has proved satisfactory in action, one centre is selected for a pilot survey. All the available patients on the list are seen, proformas are completed and an analysis made. This gives tentative answers to the questions to be determined from the research, and may suggest others. When the forms from succeeding centres are reviewed statistical comparisons should be made. If the general results agree, the work may continue; but if great variations occur, a reason must be sought.

To obtain a percentage follow-up high enough to allow reliable conclusions to be drawn, it may be necessary to complete the clinical part of the investigation by making domiciliary visits. If the whole series can be covered, this should be done; but if not, one list or group of patients may be selected, if it is large enough. If the results of this smaller more detailed follow-up correspond reasonably closely with that of the remainder, the whole may be used for further analyses. In the arthroplasty review two lists had together 160 patients of whom 145 attended for examination. I visited a further 12, and thus secured a follow-up of 98% for this group. Those I saw in their own homes were on the whole the older patients with less good results. For a survey to be accurate, it may be important to include those patients who do not come to hospital for examination.

Questionnaires sent to the patients who do not attend are not very helpful. The patient's reactions to a question by an interested person, face to face, and one on a typewritten or printed sheet are very different. In conversation a patient may express regret at the results of an operation, whereas he would hesitate to put an adverse opinion down on paper. Of the 650 patients I saw, 39 stated definitely that in their opinion the operation had not been worth while, whereas none of the 52 patients who completed and returned questionnaires gave this answer.

CONCLUSION

Clinical findings can never have scientific accuracy, but the nearest approach can be obtained by one detached observer seeing (alone) a high proportion of a large number of patients, making the same routine examination, and recording all details on identical proformas. Statistical analyses should then give reliable conclusions which help in assessing the value of operative procedures or treatment.

The investigation was carried out at the Bristol Royal Infirmary; the Princess Elizabeth Orthopædic Hospital, Exeter; the London Hospital; the Middlesex Hospital; and the Royal National Orthopædic Hospital. I should like to thank the surgeons for allowing an outsider unlimited access to records and patients, successes and failures, and freedom to report the findings.

I should also like to thank Mr. T. E. Cowan, statistician to the Middlesex Hospital, for much valuable advice; the secretaries at the various centres, whose only reward for good work was to be given more to do; the nursing staff for their assistance; and lastly the patients for their coöperation. This work was made possible by a generous grant from the Oliver Bird Fund of the Nuffield Trust.

BETWIXT AND BETWEEN

A RECOVERY HOME FOR THE OLD

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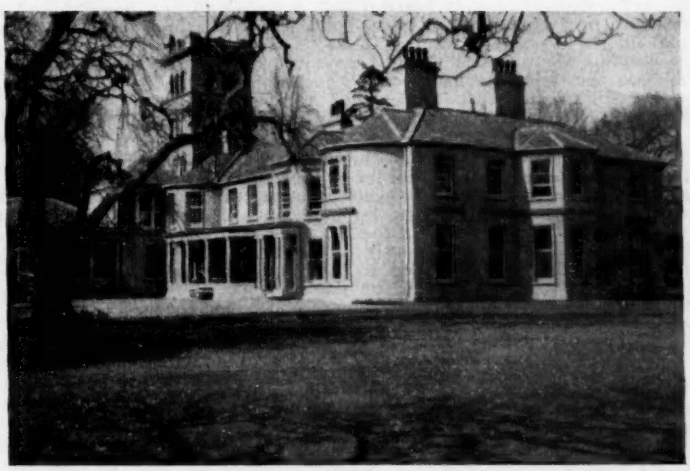
THE advantages to a hospital of a temporary "home" for patients recovered from the acute stage of illness, but still unfit to resume normal living conditions, are well known. As a recent report [1] from the King Edward's Hospital Fund points out, these recovery homes increase the turnover of acute cases at the parent hospital and reduce the waiting-list, provide an atmosphere which helps the patients' recovery, and reduce the total cost per patient. The report suggests, however, that geriatric patients are unsuitable for admission to these homes because they are often difficult to discharge. This may be true of the long-term elderly sick, but many elderly patients admitted to general hospitals for an acute illness would respond to care in a recovery home. Treatment started in hospital can be continued. The almoner, by studying the needs of each patient, can often help to overcome his domestic difficulties before his final discharge. In this way relapse and premature readmission to hospital can be avoided for many old people, who often fail to realise the toll of physical capacity and independence taken by illness until the shelter of hospital is exchanged abruptly for a life of comparative hardship at home.

Another group of elderly sick who present special problems in hospital are the so-called frail ambulant patients. Their numbers are increasing, and many are by-products of geriatric medicine, in which rehabilitation sometimes stops short of full restoration of function. These patients escape bedfast invalidism but fail to gain freedom and independence. Many have homes but cannot manage them: others have neither homes nor relatives willing or able to take them in. They do not need hospital nursing care, but they are unfit for local-authority hostels and may occupy badly needed hospital beds for weeks or months. It is difficult to allot responsibility for them to any one authority because their standards of health and physical fitness and their abilities vary greatly from month to month or even from day to day.

1. Recovery Homes. London, 1954.

The governors of the National Corporation for the Care of Old People have lately set up rest homes, where the management and care of elderly patients might be studied by the authorities responsible for them. The rest home has the same purpose as the recovery home—namely, the earlier release of hospital beds without prejudice to the recovery of the patients. The word "convalescent" is avoided because recovery homes and rest homes offer more treatment and supervision than convalescence usually implies.



THE HOME

In 1952 one of the rest homes was started at Seapark, Greenisland, co. Antrim, which was bought and equipped by the National Corporation, as a contribution to services for old people in Northern Ireland, from funds sent by the people of South Africa after the war. After consultation with the Northern Ireland Hospitals Authority and the county-council welfare committees it was decided to establish the home in county Antrim, reasonably close to the geriatric units in the Belfast City Hospital and the Braid Valley Hospital, Ballymena. To ensure proper use of the beds and easy interchange of residents who fell sick with new admissions from hospital, the corporation proposed that patients should be admitted to Seapark only from hospital geriatric units. The residents, though infirm and perhaps needing days in bed from time to time, must be readmitted to hospital if they came to need constant nursing attention in bed. Otherwise (it was feared) the turnover of patients would cease and the home become a hospital annexe of bedfast invalids.

ACCOMMODATION AND STAFF

The home opened with 25 beds, later increased to 42, and began to receive patients early in December, 1952.

There is a nursing staff of 8 and a domestic staff of 7:

Nursing	*Domestic*
Matron, Deputy matron } S.R.N.	Cook
2 State-enrolled assistant nurses	Assistant cook
3 Female orderlies	3 domestics
1 Male orderly	Gardener
	Handyman

The matron was previously a ward sister in the geriatric unit of the Belfast City Hospital and her experience of the work of the unit smoothed over early difficulties and helped to establish ready interchange of patients and continuity of treatment. The matron, her deputy, and the cook live on the premises. Day staff comprises the matron or her deputy, one nurse, and three orderlies. One nurse and one orderly are on duty at night, with the matron or deputy matron always on call.

A local practitioner and his assistant agreed to attend patients in the home for emergency calls or minor indispositions. The physicians from the geriatric units visit the home in turn each week. The successful use of the rest home depends greatly on the detailed study by the almoners of the social problems of each patient before he leaves hospital, and on their follow-up.

Local voluntary services have been encouraged to introduce diversional therapy and library services for the residents.

THE PATIENTS

Of the 42 beds available in Seapark during the year, approximately 17 were occupied by Braid Valley Hospital patients; so the following data relate only to the remaining 25 beds occupied by patients from the Belfast City Hospital.

There were 14 City Hospital patients in residence at the beginning of 1953, carried over from those admitted in December, 1952. A further 204 patients were discharged from the hospital to Seapark during 1953. 25 of these were still under treatment on Dec. 31, 1953, and the fate of the remaining 193 patients, including the 14 carried over from 1953, is set out in the table.

Patients admitted to Seapark must be able to get up daily, to dress themselves, and to walk (if only from room to room) preferably alone, or with very little assistance. Simple "cerebral incompetence" is acceptable, but mental confusion with restlessness, antisocial behaviour, or incontinence are not. Allowance is made for lapses into confusion and occasional incontinence after transfer from familiar surroundings and faces in hospital, and considerable "preparation" of the patient by the almoner is often necessary to forestall resentment when transfer is being arranged. Part of the function of the rest home is to give such patients a chance to adjust themselves to a change while still under supervision. Despite every effort, several patients have returned home prematurely rather than face the rigours of rural life, twelve miles from Belfast. Old people are equally perverse in their refusal to fall neatly into administrative categories, and this is borne in mind when they are transferred to Seapark in one of the following three groups:

Group I: Supervised Convalescents are patients who are transferred to Seapark earlier than they would normally be sent home. The most common disabilities of this group were hemiplegia, fractured femur, and debility due to malnutrition and poor home conditions. There were 94 patients in this group (26 men and 68 women) and 90 of them returned to their homes or to residential care, fully independent. 4 had to return to hospital after a relapse, of whom 2 died. The average time in hospital was forty-two days for women and 24 for men, plus an average time in Seapark of 28 days for women and 24 days for men.

Group II: Assessment.—The patients in this group were mainly women. Their reaction to discharge from hospital was hard to assess. Some showed physical or mental instability and lack of confidence. Others were beset by social problems—unsuitable homes and no

FATE OF PATIENTS AFTER DISCHARGE

—	Home	Lodgings or residential home	Returned to hospital		Total
			Long-stay	Died	
Group I ..	79 (84%)	11 (12%)	2 (2%)	2 (2%)	94 (100%)
Group II ..	30 (52%)	13 (23%)	11 (19%)	4 (6%)	58 (100%)
Group III ..	7 (17%)	14 (34%)	15 (37%)	5 (12%)	41 (100%)
All groups	116 (60%)	38 (20%)	28 (14%)	11 (6%)	193 (100%)

apparent alternative to a hospital bed, a spouse ill in hospital, or a companion help on holiday. Of the 58 patients (12 men and 46 women) 15 (25%) had to return to hospital where 4 died within the year, but Seapark released the beds they had occupied in hospital for an average of two months. 30 returned home and 13 to lodgings or hostels.

Group III: The Frail Ambulants.—41 elderly patients, who had nowhere to go, though they no longer needed hospital care, were looked after in Seapark during the year. Their average stay was seventy-seven days, but several patients had been there for many months, one for eight months. About 10 of the 25 beds used by the City Hospital were continuously occupied by these people. Half this group had to return to hospital eventually, and 5 died during the year. Homes were found for 21 of them after prolonged efforts by the almoners.

A YEAR'S WORK

The rest home thus relieved the geriatric wards of 152 group I and group II patients several weeks before they would otherwise have been discharged. The liability to premature breakdown and readmission to hospital was lessened by the gradual transition in Seapark from hospital to home conditions, and time was given to ensure proper resettlement. The readmission-rate of the geriatric unit fell from its usual level of 12 to 8% in 1953. 41 frail ambulant patients were also cared for in Seapark for two or three months. As the average time in the geriatric wards of remediable acute admissions is thirty-three days these patients released hospital beds for about 82 new admissions. The average days in hospital for patients discharged home as recovered, fell from forty in 1952 to thirty-three in 1953, and there were 826 admissions in 1953 compared with 644 in 1952, an increase of 28%. The effect on the waiting-list is less obvious because it is a list of chronic cases, none of whom would ever be suitable for admission to Seapark, and it reflects the shortage of long-stay accommodation in the area. As a result of this shortage the unit tends to increase the number of long-stay beds at the expense of active beds. Seapark encourages this trend by enabling a better turnover of the smaller number of active beds, but it must be opposed, because at least 35 active beds in the unit are needed to keep 15 in Seapark fully occupied. A rest home cannot make up the deficiency in long-stay beds in the area, though it does much to forestall the growing demand for them.

The advantages to patients of a period in Seapark are beyond question, especially for those whose illness or disability has been aggravated, or precipitated, by prolonged loneliness, malnutrition, and neglect. Several patients who recovered unexpectedly in hospital from serious illness seemed to "hang fire" until transferred to the rest home where their mental and physical improvement and renewed confidence, vigour, and interest in living showed how the atmosphere of the home speeds recovery.

The benefits to the local authority are indirect, and perhaps more real than apparent. Seapark enables patients to adjust themselves to residential care before transfer to a hostel. Some infirm old people for whom no alternative accommodation exists, and whose problems are essentially social rather than medical, are being looked after. Others return home more fit and able to fend for themselves, and less in need of the domiciliary services than if discharged direct from hospital.

As Seapark was completely renovated before it was opened maintenance costs so far amount to little. The home has been run efficiently with its present staff, but any change in the ratios of the three groups of patients, or the development of more skilled physiotherapy and craft work, would necessitate more staff and some more money. A rough estimate of the cost per patient week is less than £5—considerably less than the cost of a hospital bed and little more than that of care in a residential hostel.

The apportionment of this cost is being settled between hospital authorities and local authorities. Both parties benefit from the home, but the gain in efficient use of hospital beds is more evident than the advantages to a local authority reluctant to recognise responsibility for the infirm.

SUMMARY AND CONCLUSIONS

The Seapark rest home combines the functions of a geriatric recovery home with those of a hostel for frail ambulant patients. In 1953, 204 elderly patients were admitted to the 25 beds available to the geriatric unit of the Belfast City Hospital. They fell into three groups: those needing further supervision and treatment (average stay of one month); those admitted for assessment of future capacity (two months); and frail ambulant long-stay cases (three months or more). Most of them were able to return home or to hostels, including many who made unexpectedly good recoveries in the atmosphere of the rest home. Half of those in the third group returned to hospital long-stay wards.

In 1953 the rest home increased the turnover of the geriatric unit by more than 20% by reducing the average patient-days in hospital. It contributes greatly to the recovery of many elderly patients to the advantage of both hospital and local authorities. Its success depends on the careful selection of patients, and, as the King's Fund report emphasised, the home must not be used to take patients merely because they are an inconvenience to the hospital.

USE OF HOSPITAL BEDS

No new hospitals have been built since 1945, but there has been a considerable increase in the number of patients admitted to the same or smaller numbers of beds in hospitals. Some indication of the extent of this increase is given by a report from the Manchester Regional Hospital Board.[1] If in 1953 the rate of turnover had been the same as in 1949, five additional 500-bed general hospitals would have been needed in the region for the inpatients who were treated during that year.

This report includes the following comments on the various indices of the use of hospital beds:

"*Bed Occupancy.*—The average daily number of occupied beds is obtained by dividing the daily number of in-patients by the number of days in the year. Unfortunately, it is not uncommon to attach too much importance to bed occupancy and to assume that a high bed occupancy figure indicates efficiency. This can be entirely misleading and, indeed, the reverse may be true. If patients are detained longer than is necessary and fewer patients are admitted, or if they are admitted too early because there is a vacant bed, the hospital or ward would have a higher bed occupancy figure but would not necessarily be efficient. On the other hand, it is self-evident that if the turnover increases but the interval between the discharge of one patient and the admission of the next remains the same because the management cannot speed up this process, in other words if the hospital or unit becomes more efficient by reducing days in hospital to a minimum and thus securing a shorter stay in hospital for its patients, then the bed occupancy will be less. Bed occupancy figures are of little use at regional level, but they should be of interest to medical, nursing and administrative staff dealing with the day-to-day problems of ward, unit and hospital management. They should never be considered in isolation and without regard to other factors.

"*Turnover Index.*—The 'through-put' per bed or 'bed use factor' is obtained by dividing the total discharges and deaths of a particular group of patients by the number of beds in use and can be calculated over any given period, preferably one year. There are several fallacies but it can be a useful index. To increase the turnover it is necessary to reduce either the average duration of stay or the turnover interval or both.

1. Manchester Regional Hospital Board: Abstract of Statistics for Year ended Dec. 31, 1953. Published by the board, Cheetwood Road, Manchester, 8.

"*Average Duration of Stay.*—This is a useful index if properly calculated. The *true average duration* is obtained by adding together the days spent in hospital and dividing by the number of patients involved, both discharges and deaths. The *crude average duration* is obtained by multiplying the number of beds by the days in the year and dividing by the deaths and discharges. Alternatively, it is the days in the year divided by the 'turnover index.' The crude average duration does not take into account those days when the beds are unoccupied and it follows that it is always higher than the true average duration. The difference between the crude and true average duration is the *turnover interval*.

"*Turnover Interval.*—This is the interval in days between the discharge of a patient from a bed and the admission of the next. The turnover interval in the general hospitals in England and Wales in 1951 was 3·26 days and the Ministry of Health have pointed out that if this could have been reduced by one day, 93,000 more patients could have been dealt with, which is equivalent to 4,800 beds at the present rate of user. If the average duration of stay as well as the turnover interval could each have been reduced by one day, the increase would have been equivalent to an additional 17,000 beds.

"*Waiting Period Index.*—Waiting list figures are very unsatisfactory. They do not usually indicate the real situation and frequently they are not up to date. Some patients on waiting lists may conveniently wait for many months, whereas others must be admitted in a few days. If, however, the number on the waiting list is divided by the annual deaths and discharges, a figure is obtained which indicates the average waiting period as a fraction of a year. The smaller the figure the shorter the average waiting period. Waiting lists should always be compared with turnover. It is not unusual, for example, for people to refer disparagingly to the hospital service and quote the thousands of cases waiting for the removal of tonsils and adenoids. They forget that many more thousands are operated upon each year."

Occasional Survey

EXPERIMENTAL DEEP HYPOTHERMIA

As long ago as 1881 Horvath [1] drew attention to the fact that certain mammals, including the ground-squirrel, the hedgehog, the hamster, and the bat, can survive artificial cooling which lowers the deep body-temperature nearly to 0°C and that they recover spontaneously in a warm environment; but other mammals which do not hibernate are usually killed by cooling which lowers the rectal temperature to between 10° and 19°C. Since that time, hibernation has been much investigated, and experiments [2 3] have been designed to elucidate the physiological mechanisms of adaptation and the processes that differentiate hibernators from non-hibernators. The marmot has been widely used in these studies, which include that of Benedict and Lee [4] on the physiology of this species. It is a fundamental characteristic of hibernating mammals that, irrespective of a low environmental temperature and a low body-temperature, any adequate stimulus will initiate arousal, so setting off a train of physiological events leading to a striking rise in both metabolic-rate and body-temperature.[5]

The infants of non-hibernating mammals are much more resistant to cooling than adults of the same species. For example, rats within the first ten days of life will recover on subsequent warming after being chilled to temperatures as low as 2·5°C [6]; heart-beats disappear between 9° and 3·5°C and the metabolic-rate is zero at 3°C. For adult rats, by contrast, the median lethal temperature from which the animals will recover of their own accord on warming has been found to be about 15°C.[7 8] But the general belief, most recently upheld by Adolph,[7] that death is inevitable if the rats are cooled below this temperature has been dispelled by Andjus [9] at the institute of physiology of the University of Belgrade. Using special methods of cooling and rewarming, he has demonstrated that adult rats may be fully revived after their rectal temperatures have been lowered as far as 1°C. The animals were cooled in two stages: first, they were confined in small containers so that they could be exposed to a progressive fall in oxygen tension and a rise in carbon-dioxide tension; and the containers were placed in a refrigerator. When their temperature had fallen to about 20°C and they had become lethargic, the rats were taken out of the containers and further cooled by covering them with crushed ice. In this way their colonic temperature was reduced as far as +1°C. Respirations ceased below about 9°C, but the heart continued to beat until the temperature had fallen below 6°C. As others had previously found, Andjus was unable to revive rats so cooled merely by rewarming the body and carrying out artificial respiration. He found, however, that if the circulation was first re-established by applying heat *locally* to the cardiac area (by putting a heated metal object on the skin or by means of a beam of light [10]), combined with artificial respiration, then the risk of anoxia during the rewarming process is reduced and recovery is possible. The heart began to beat again when the temperature had risen to 5°C and spontaneous respiration was restored when it had reached 15°C. Only when both cardiac action and respiration had become regular was the entire body finally rewarmed by immersion in warm water at 40°C, and consciousness then returned. It is reported that reanimation and survival regularly followed cooling to 7–9°C, but after reduction of the temperature to +1°C, although reanimation was regularly achieved, it did not usually last long. Nevertheless, in certain instances, the animals survived, even after the cessation of both respiratory and cardiac activity for as long as one and a half hours.

A recent paper by Smith, Lovelock, and Parkes,[11] of the National Institute for Medical Research, has now extended the knowledge of the capacity of mammals to withstand extreme cooling. They have been studying the survival of hamsters whose body-temperatures were reduced to below zero. These animals were chosen because, being hibernators, they are normally adaptable to a wide range of body-temperatures. On cooling hamsters by Andjus's method, respirations ceased between colonic temperatures of 2·5°C and 6°C and the heart-beat stopped at temperatures varying from 1·8° to 3·5°C. Recovery after a temperature of 2°C was not spontaneous, though it was readily brought about by Andjus's technique. By transferring animals, previously chilled to the point at which respirations had ceased, to a 50% propylene-glycol bath at −4° to −6°C their colonic temperatures were reduced to zero in seven to ten minutes. Under these conditions supercooling took place in some of the hamsters, the temperatures falling as low as −5·5°C. When such animals were taken from the bath, while they were still supercooled (at −3° to −5°C) and flaccid, heat and artificial respiration revived them completely. In other animals, however, the process of supercooling ended abruptly when the colonic temperature rose suddenly to about −0·5°C, although they were still immersed in the cold bath. Stiffening began simultaneously, indicating that some of their body-water was crystallising. In these animals complete recovery was rare, though cardiac function could be restored. Peripheral freezing began in the majority of hamsters cooled below zero, the colonic temperature remaining steady at about −0·6°C. As ice formed, they stiffened progressively until they were "wood-like to the touch"; presumably they consisted of hard, frozen shells surrounding unfrozen

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11. Smith, A. U., Lovelock, J. E., Parkes, A. S. *Nature, Lond.* 1954, **173**, 1136.

or only slightly frozen interiors. Although animals subjected to fifteen minutes' freezing under these conditions could be completely revived by Andjus's method, imperfect recovery resulted after a longer period of freezing. Nevertheless, by the application of modified methods, including diathermy for deep and rapid heating of the entire body, Smith et al.[11] report that they have fully revived animals frozen for as long as thirty-eight minutes. They point out that, in animals which survived peripheral freezing and "whose ears attained the consistency of cardboard," damage attributable to this cause was rare; but it should not be forgotten that mammalian skin is remarkably resistant to freezing and thawing.[12] The current investigations include methods of resuscitation and rapid cooling through the crystallisation zone.

Much is now known about the conditions under which a wide variety of mammalian cells and tissues,[13 14] and possibly organs too,[15] will withstand long-continued freezing at the temperature of solid carbon dioxide, −79°C, or of liquid air. After storage in what amounts to a state of totally suspended animation and subsequent thawing under the appropriate conditions, critical functional biological tests have shown the cells and tissues to be none the worse for their ordeal. The possibility that it may eventually be feasible to store a whole animal (perhaps a man) in a similar way may seem attractive to some, though its ultimate realisation is very far from certain. A great deal has been learnt about the capacity of cells and tissues to withstand very low temperatures, but much more information is needed about the capacity of the animal as a whole.

Before Our Time

LOCKE'S MIDWIFERY NOTES

KENNETH DEWHURST
B.Litt. Oxfd, L.R.C.P.I.

John Locke's attainments in the realms of philosophy, theology, and practical politics have received such wide and just acclaim as to completely overshadow his other activities. The man who first drafted the Constitution of Carolina, the author of *An Essay Concerning Human Understanding* and treatises on Toleration, Government, and Education has earned more enduring claims to posterity than Locke the physician. Indeed, Locke's medical associations were described as "loose and uncertain" until the appearance of Fox-Bourne's biography in 1875 when it was first realised that he had at times been an active practitioner who had assisted Sydenham in his investigations of smallpox; that he had operated on the Earl of Shaftesbury for a hydatid abscess of the liver; and throughout the whole of his long life had always been ready to treat cases and give advice. It is tempting to speculate as to how much mankind would have at once lost and gained; how much philosophy would have been retarded, and how greatly medicine would have been advanced had Locke stuck "to the physic line."

HIS LIFE

John Locke was born in 1632 at Wrington in Somerset, eight years after Sydenham and ten years before Newton. He was educated at Westminster School and Christ Church, Oxford, where he was successively lecturer in Greek, Rhetoric, and Moral Philosophy. Unlike his fellow dons, Locke did not take orders: instead he interested himself in medicine, and, following a journey to Brandenburg in 1665 as secretary to Sir Walter Vane, he began to practise in Oxford with Dr. David Thomas. His contemporary, Anthony Wood, writes: "Mr. Locke having gone through the usual courses preparatory to practice entered upon the physic line and got some business at Oxford." It seems most unlikely, however, that he had "gone through the usual courses," for, in 1666, Lord Clarendon, the Chancellor, proposed that Locke might be allowed to accumulate the degrees of M.B. and M.D. His request was refused and it was not until 1674 that Locke became a bachelor of medicine, six years after his election to the Royal Society. He never proceeded to a doctorate.

Locke's first services to Lord Ashley (afterwards Earl of Shaftesbury) were purely medical. He procured some medicinal water from Astrop for his lordship, and, shortly afterwards, was installed as physician to the Ashley family. In the following year (1668), Locke became friendly with Sydenham whom he assisted in his research on smallpox. "I perceive my friend Mr. Locke," writes Sydenham to Boyle, "hath troubled you with an account of my practice as he hath done himself in visiting with me very many of my variolous patients especially."

In the same year, Locke treated the Countess of Northumberland for trigeminal neuralgia, of which he gives a classical description in his letters to Dr. Mapletoft, professor of physic at Gresham College. He returned to England when Shaftesbury was again in power from 1679 to 1684; but after his patron's death Locke himself came under suspicion of having plotted against the Crown, which necessitated a six-year sojourn in Holland. After the Revolution, Locke returned to England where he devoted his energies to literary and political work until his retirement in 1700. Until his death, four years later, he interested himself in medicine (as much as his health would permit) and gave advice to the neighbouring poor.

THE NOTES

In 1947, the Bodleian Library acquired a large collection of Locke's papers from the Earl of Lovelace. Amongst the many letters, notebooks, and essays of medical interest are these notes[1] on midwifery (written about 1695):

"If she be with child let her not doe as is usuall with women of condition shut herself up in her chamber for fear of miscarrying much less confine her self to her bed. This makes the body and spirits weak which is one great cause of miscarrage to which the constant fear of miscarrage which this management keeps constantly upon the mind of the breeding woman upon any slight accident joyning it self seldom fails to produce an abortion. For the minde being kept in a constant apprehension of miscarrage every the least occasion turne that apprehension into a viall fright and what that produces in teeming women experience tells us. Hence we see that amongst the poor and labouring country women not one of ten miscarry in comparison of the aborting to be found amongst people of quality. The phansys of these last being by chat of visitants and the inculcating of rules set on worke with tea, and their bodys kept lazy and without exercise, strength is added to what hurts and threatens if withdrawn from what support and continues the fœtus in the womb.

'HER ORDINARY COURSE'

"Also it becomes unnatural and extraordinary for a woman of quality to go out her time as it is natural and ordinary for a common ordinary woman to miscarry. If therefore she be with child let her continue her ordinary course of living and exercise as if she were not without any apprehension, yet nature intended that women more than any other creature preferably upon their conception should presently change their whole course of life and be perfectly idle and lazy for ten months together; as the burden they carry begins to be sensibly too heavy for them then they may think nature advises them to ease and abatment of exercise till then they need apprehend nothing from the motions of their ordinary business—only these two must be avoided: first lifting of great weights beyond their strength which being a stress of labour belongs not to their sex. The other is to remember not to lift their hands higher than their heads thereby to accustom themselves not to reach at anything above them

12. Billingham, R. E., Medawar, P. B. *J. exp. Biol.* 1952, **29**, 454.
13. See *Lancet*, 1953, ii, 26.
14. Smith, A. U. *In* Biological Applications of Freezing and Drying. New York, 1954.
15. Parkes, A. S., Smith, A. U. *J. Physiol.* 1954, **123**, 67P.

1. Locke MS. c. 29, folios 95–98.

which in breeding women is often of very ill consequence. All other moderate exercise especially in the open air is for the advantage both of mother and child as may be observed in the labour and offspring of poor labouring people that are pinched under the difficulty of necessity and want, for they and their births suffer another way.

Next let her diet be ordinary plain food such as her stomach takes best and not such as is recommended by the most useless nicety of others. But only spice of all kinds and high sauces are to be avoided. And as to drink the smallest is always the best, unless custom has made stronger liquor necessary and then it is not wholly to be broken off of a sudden, but gently to be quitted and by degrees, as the stomach and fancy can be brought to consent. But this is to be *observed in drinking of all sorts that they be fine and quiet,* no burliness, lee or fret in them.

If she has at any time before miscarried as in the third, *fourth or any other month besure a little before that time* to let blood in the arm as much as the strength and constitution of the patient will well bear: and let it be done with these circumstances. In the morning in her bed and taking after it as soon as her arm is bound up again an ounce of diacodium in three ounces of cowslip water and then let her compose herself to sleep again, somebody sitting by her all the time of her sleep to watch that she does not hurt *herself on the side she was bled and so lying on the blouded* arm by compressing the vein which may open set it fresh on bleeding which is all ye danger in sleeping after being *let bloud. The same remedie of bleeding must be used in* the same method if she finds the child at any time bustling and disordered; any tendency toward miscarriage by any fright, fall or any other occasion.

'HEED OF FORWARD HANDS'

When the time of the birth draws near let not her be too forward to put herself into labour; nor her midwife be too busy with her. Those for the most part are meddling but ignorant women who think they must be doing something that they may not appear useless and unskillfull, though it be generally to the prejudice of the great bellyed woman who by the officiousness of ye midwife being put upon labour before the child is full ripe for the birth, have their strength wasted before the time that they should bring forth, and so both mother or child or both perish under it. The natural birth is a work only of nature which only knows when the fruit of the womb is full ripe, and if it be let alone till that time it drops as it were of it self it is certain it comes easiest. The way therefore to be soonest, easiest, and safest brought to bed is to avoid the labour of childbirth and decline the thought and ways of being relieved as long as you can and not presently to put yrself upon it upon the first pains and tendency to it. Nature cannot be much hastened at least safely in this work. And when it is the time (if the strength hath been preserved from hasty tampering) cannot be delayed; and therefore to be heed of forward hands and forceing medicines.

At the time of labour let not the room be crowded with useless women; so many and no more as will be of use to the woman in labour are all should be there; all the rest hurt and hinder one another and spoil the air of the room which is the great refreshment of the woman in labour. As the open air is of great use to a breeding woman so nothing is so dangerous to her as soon as she is delivered, and therefore she should be immediately had into bed—nay the best way is to be delivered in bed, but the fashions of countrys are not easy to be altered. As soon as she is well laid and it is fit for her to eat anything let her have a boiled chick if her stomach will bear it. Eating flesh in childbirth supports the strength and is better especially for this lady than a lower diet, but then it must be begun the first day and so she must eat a chick everyday for if it be forborne the first day and attempted afterwards it produces a feavor and often death.

In her lying let her avoid seeing much company and all talking very careful and every thing else that may raise vapours, for these are dangerous in her case, for they will stop the course of nature and drew after them a new train of obstructions; but if she be well laid and all things go on well in this lying in as they should and she have a due care the two or three months following, nature will again take to its own regular course and all will be well."

Though their style is somewhat whimsical, these notes contain much simple and sound advice.

In England Now

A Running Commentary by Peripatetic Correspondents

A CLOUDY day had given place to a murky evening: a thin mist enshrouded all but the tallest cranes which brood over the Clyde. As I walked home and reflected on the imminence of autumn I was suddenly startled by a woman's screams. I ran round the corner and there she was—a matronly Glaswegian in her Sunday best, gesticulating and shrieking abuse at the retreating figure of a young man. The situation was obvious at a glance: he was a bag-snatcher. I gave chase, and he darted off across the tram-lines and down the next side street. Something evidently checked him for when he came in sight again I found myself only twenty yards from my quarry. Suddenly he vanished down a close. I followed, knowing that he would avoid trapping himself on the staircase and would almost certainly emerge by the back door. I was right: away he went over the drying-ground littered with dust-bins and mangy cats and so back to the street. "It's a long time since I ran like this," I thought, "but I'll show this young hooligan. . . ." On we went, sometimes on the pavement, sometimes on the road, and I was vaguely aware that pedestrians had stopped to watch the chase. After two or three minutes we were back to where we started: a little crowd had gathered around the woman—now weeping noisily. I was still twenty to thirty yards behind the thief, yet try as I would I failed to reduce the gap. The pedestrians along the course seemed to have increased in number. The sweat coursed down my face and my linen collar was now firmly plastered to my neck. "The tram lines again," I grunted. But this time there was a tram also. The bag-snatcher took a chance and ran in front of the tram; but I had to wait for a gap in the traffic, and when my chance came the thief had vanished. Had he cleverly boarded the passing tram or had he been sucked into the earth by that satanic mist?

I wandered back rather aimlessly, and my exasperation gave place to indignation. The citizens who had stationed themselves on the kerb as spectators were beginning to move again, but I thought I would tell at least one of them what I thought about him. I walked towards one fellow standing there like a monument clad in belted mackintosh, flat bowler hat, and square-toed shoes. Before I could frame a suitable rebuke, he fixed me with his dark eyes, removed the pipe from his mouth, and spat with great deliberation: "Man," he said, "ye nearly had him the second time round."

* * *

My holiday intention this year was to forget all about medicine. So I travelled to a foreign land where I hoped that a strange language and strange customs would protect me from my profession. But I had scarcely arrived when my colleagues sought me out, and before long we were clustered together in a little clinical conference. The symposium consisted of a general practitioner from Holland, whose chief assets were the sound common sense he brought from his country practice and the diverting vivaciousness and charm of his two daughters; a chest physician from Alsace with whose wisdom I could barely keep pace, though I became expert in flipping the pages of my dictionary; and a gynæcologist from Belgium, who, for obvious reasons, found himself at a diagnostic disadvantage.

We regarded ourselves as well equipped to discuss the clinical aspects of our fellow guests. The affectionate little girl with protruding tongue and pink eyelids, we all agreed, was a mongol. The head waiter probably had alcoholic cirrhosis, but he was a nice chap and we unanimously accorded him a good prognosis. The old fat lady, who shuffled about painfully with two sticks, proved more difficult. Rheumatoid arthritis seemed likely, but she always sat outside, in sunshine or rain. The suggestion that she might be the surgical success of a pinned fractured femur was applauded. The slate-blue discoloration of the face of the gentleman dining in the corner aroused lively interest. I was in favour of sulphæmoglobinæmia—mercifully almost the same word exists in French and Dutch. The fact that the colour seemed less pronounced on the day after we had spinach for dinner was held not to be without significance. The

Dutch doctor had little support for his diagnosis of argyria, but, unlike the rest of us, he had seen a case. Even psychiatric problems came up for our consideration, and we all agreed that the exuberant gentleman who went for a swim at 6 A.M. each morning, and played ferocious pingpong after every meal, could take a thrice-daily dose of phenobarbitone with advantage.

We also enjoyed discussing natural conditions of work and exchanging nomenclature. I was interested to hear that the Continental physician is called a specialist of internal diseases, and my colleagues were astounded to learn that, under our beneficent health service, most of the patients I now see have no disease, external or internal.

* * *

I remember having a conversation some 25 years ago with a Cornishman who thought his county was not particularly beautiful (as well he might for he lived in Bodmin); but he added, "There is nothing to beat a Cornish lane." I thought of him again as I picked blackberries from one this summer.

The myriad of stones which form the walls are there, I suppose, because it was the easiest way of stacking them when they were taken from the fields, which would certainly be unproductive if they remained there. Nine tiers of stones; a span each is a usual formation, and, as each stone is often less than an inch broad, in some places there must be over 3000 stones to a yard, and double that for both sides. The loose earth between the stones nourishes a profusion of wild flowers, the gorse with its prickly stalk and bright yellow flower, and the red heather standing erect, the wild poppy, mustard, toad-flax, scabious, bladder-campion, knapweed, tansy, and lady's bedstraw sticking their heads sideways, with their yellow, purple, red, and green shades which would make a lovely design for a carpet. Perhaps a yard away, ferns grow in abundance in every shade of green, and, lastly, thyme with its delicate pink and delectable smell. I have put it last, not because it is the smallest but because it might perhaps go unnoticed if it had no scent. Did Shakespeare put it first because his sense of smell made him notice the bank, and then his roving, observant eye picked out the others? Picking blackberries in a Cornish lane from the top of a bank which they shared with blue sloes and scarlet hawthorn berries made me realise how truly Bacon wrote when he said, "God Almighty first planted a garden." Wilderness still has its charm.

* * *

Our Peripatetic Parliamentary correspondent writes: In the passage by the House of the second reading of the National Health Service (D.D.) Amendment Bill as an agreed measure, an important step has been taken to close a gap in our system of social security. In moving its adoption, the Minister of Agriculture and Fisheries said he was proud to be associated with a measure which would provide every type of health care for the Darling Doggies. It had long been felt anomalous that in this country, which had pioneered so many social advances and which abounded in D.D.-lovers, the welfare of our four-footed friends still depended as much on private and voluntary effort as in the days of Gellert and Hodge. (A hon. member: Hodge was a cat.) He apologised, Crichel had rather got him Down, he should have said Flush. All kennels in the country, with the exception of disclaimed dog-baskets, would be administered from the Appointed Day by regional, group, and local kennel boards and committees. In view of the importance of nutrition to health, bones would be provided free of charge or at cost price through the maternal and puppy welfare clinics. Thanks to his friends the bloodhounds, no inroads would be made on the existing transfusion services. He hoped that the day had dawned when the phrase "a dog's life" would take on a new meaning, and he felt sure that hon. members of all parties would metaphorically lift their hands—he had nearly said legs—in support.

* * *

From the Anglo-Saxon Chronicle for the year A.D. 1086—"It was a very severe year, and a very sorrowful year in England; and corn and crops were checked, and there was such great misfortune with the weather as cannot easily be conceived. There were such big thunderstorms and such lightning, so that many people were killed, and it kept getting worse and worse among the people, more and more so. May God Almighty make things better."

Letters to the Editor

LUMBAR PUNCTURE IN POLIOMYELITIS

SIR,—Your correspondents deprecating the performance of lumbar puncture in cases of poliomyelitis seem to have allowed their enthusiasm to outrun their discretion. By all means let us dispense with lumbar puncture when paralysis has occurred and the diagnosis is certain, though one may still be deceived by the occasional Guillain-Barré in which sensory signs are minimal or not looked for.

But in so-called abortive poliomyelitis the situation is very different. Briefly, in this country at the present time, a patient presenting with acute neck and back stiffness usually has: (1) poliomyelitis; (2) incipient meningitis (coccal, bacterial, or leptospiral); (3) any of the other viral meningo-encephalitides (including perhaps glandular fever and erythema multiforme); or (4) subarachnoid hæmorrhage.

What is one to do then? Is it suggested that one should wait, thereby wasting precious, and it might well be vital, time until some unmistakable clinical development forces one's hand; or attempt by means of lumbar puncture to make a differential diagnosis at once? The latter is the course which, in my view, one is bound, in the patient's interest, to follow. (Incidentally, if the waiting policy were widely adopted, subarachnoid hæmorrhage might rarely be diagnosed during life.)

In any event the large number of cases of non-paralytic poliomyelitis that come into hospital, undergo lumbar puncture, and depart unscathed must surely suggest that the occasions when puncture precipitates paralysis must be exceedingly few. Moreover, the large measure of common agreement between the ratio of non-paralytic to paralytic cases in outbreaks all over the world again suggests that puncture can have no very decisive influence in altering the balance. The question was debated briefly at the first poliomyelitis conference held in New York in 1948, when the majority opinion ran counter to your correspondents' views.

Finally, are we not becoming a little too "poliomyelitis conscious"? At this hospital, in striking contrast to previous years, we have had only one case of paralytic poliomyelitis since January. Two "bulbars" proved to be examples of Guillain-Barré syndrome. Moreover, the majority of the "abortives" would seem to have been mumps, as shown by subsequent clinical developments, or suggested by the findings in the fluid, complement-fixation tests, and/or a significant rise in the serum amylase.

I must apologise for stressing the obvious but it would be intolerable if your correspondents' contention—that it is bad practice to do a lumbar puncture in cases of suspected poliomyelitis—were to be generally accepted and perhaps subsequently quoted against us in courts of law.

South Middlesex Hospital, Isleworth. G. E. BREEN.

SIR,—Your correspondents are to be supported in their views that undue interference and disturbance in dealing with the poliomyelitis patient in the preparalytic stages of the disease is to be deprecated, and that lumbar puncture in the case where diagnosis is without doubt should best be omitted. I know of no statistical evidence, however, to support the theory that lumbar puncture is a factor precipitating paralysis, and, indeed, experience in this hospital has never given rise to any suspicion of such a reaction. There have been a great many instances where the operation was performed in non-paralytic cases in the meningeal phase and where no paralysis followed. The unpredictable nature of this disease must make untenable any argument that where paralysis followed or increased the cause must be the lumbar

puncture. As a corollary, it must be as logical to attempt to accept that, where patients with clinical evidence of poliomyelitis received neutralising antiserum and did not develop paralysis, this happy state must be attributed to the serum.

Those of us with diagnostic units have much opportunity to observe the diseases admitted as suspected poliomyelitis and know only too well how common it is to meet cases with a meningeal reaction clinically indistinguishable from the preparalytic phase of that disease. The information gained from a diagnostic puncture has been invaluable in allowing early and life-saving treatment to begin in many cases of tuberculous and septic meningitis. Conservatism, as advocated by your correspondents, will almost certainly lead to many tragedies.

Dr. Albury advocates "specialists" for lumbar puncture. This is obviously impracticable. The operation of lumbar puncture can be efficiently performed with minimal trauma or discomfort by those who have been instructed in the correct technique and have the right equipment.

The Western Hospital,
London, S.W.6. W. HOWLETT KELLEHER.

DRUGS THROUGH THE LETTER BOX

SIR,—As a household containing two doctors, we are inundated with medical advertisements.

As the letters drop on the doormat, they are pounced on by the children, to be distributed to their owners. All advertisements are counted as the children's "spoil," to be used for cutting out or learning their letters. We find this a satisfactory arrangement and only occasionally salvage a blotter, as we need one.

Sometimes this peaceful state of affairs is disrupted by the arrival of samples of drugs by letter post. We have trained the $3^1/_2$-year-olds never to open packets of pills or to taste any, so they obediently hand them to us and watch wonderingly while we flush them down the lavatory. Now that our youngest is crawling, the problem has struck us again with renewed strength and we are driven to ask if nothing can be done about what is, in effect, a recurrent peril to medical households with children. Could not all drug manufacturers agree to send a card, to be returned by those who require samples? Or will it be necessary to press for legislation to prevent the mailing of dangerous drugs to unwilling recipients?

London, N.3. SUSANNA ISAACS.

THE HUMALACTOR

SIR,—May I reply to Dr. Waller's comments (Aug. 21) on the humalactor? I start with a disclaimer: this invention, called by Dr. Waller "Dr. Gunther's contraption," is in no way mine and I have no connection with it whatsoever beyond trying it out and finding it useful. Medical inventions of all kinds—drugs, devices, and methods of management—deserve dispassionate appraisal and this I had sought to provide for the humalactor in my brief article on its use.

Dr. Waller does not like the humalactor and sees in it a deterrent to the training of midwives and mothers in the technique of manual expression of breast secretion. No-one should fail to recognise the great contributions Dr. Waller has made to understanding the nursing mother and the processes of breast-feeding; yet, while paying tribute to all he has done and to Dr. Waller himself, with the affection and respect which years of friendship have strengthened, I have thought it right to try other methods. Hospitals differ in their resources in personnel and also in the cases they receive. Many women find manual expression repugnant and, certainly, some nurses should not be taught, neither should they practise, manual expression on mothers in the early puerperium, when breasts are so tender and easily injured. Our mastitis rate has, in fact, risen on each of the four occasions when we have introduced frequent early manual expression. Because of this failure and because early engorgement causes much suffering, alternative methods shortly to be described are used to reduce the incidence of engorgement of the breasts in this hospital—hence the relative smallness of the volumes of surplus milk removed by the humalactor.

The severest censure in Dr. Waller's letter is that reliance on a machine will render midwives and doctors content to let the patients manage as best they can when they go home. To me this is an illogical conclusion and an unjustifiable charge. Midwives are not made more considerate by being driven to perform hurtful practices on difficult and engorged breasts, nor does recognition of the tenderness of breasts in the first week prevent a nurse or doctor from providing mothers with means to empty their breasts if necessary later. We find that if engorgement is avoided and if the department does not glory in the numerical pride of excess milk, most mothers go home contentedly and adequately feeding their babies and seldom have to do more than keep a watchful eye for excess secretion. Nor are failures as common as Dr. Waller's reckoning would suggest: the humalactor, when we had only one machine, was used on those who had difficulties. At present we try to teach mothers the skill of manual expression before delivery and rely on the method where we deem necessary, but not, if we can help it, before the fifth day.

The humalactor's characteristics seemed worth describing since they differ happily from those of all other breast-pumps I know. I would agree with Dr. Waller's matron that these others can stay unrepaired, or, where I have so often seen and left them, "lost" in a cupboard.

Obstetric Hospital,
University College Hospital,
London, W.C.1. MAVIS GUNTHER.

TERMINOLOGY IN LACTATIONAL PHYSIOLOGY

SIR,—On Sept. 7, the British Association is to hold a joint session of its agriculture and physiology sections, and the subject has been announced as The Physiology of Milk Liberation. The discussion will deal with the reflex which causes movements of milk from secretory alveoli in which it is stored to duct spaces near the teat, which occurs when the baby animal feeds and which is known as the draught reflex in women and as the let-down in cows.

We think that the new term, "liberation," is an unsuitable word for this process, for it suggests that the milk is held back and then released, and the term brings to mind a relaxation of a sphincter or the escape of the secretion across a membrane. We think the term "ejection," introduced in a valuable extension [1] of Folley's excellent scheme [2] setting out the phases of lactation, is also unsuitable, because milk is but rarely ejected, although the pressure within the duct is increased by the reflex. The same consideration applies to the term "expulsion."

"Propulsion" seems to us to be preferable to any other of the terms so far suggested, for it connotes an active transportion of milk, it is without misleading implications, and it is widely used in the practice of human lactation. We think its general acceptance would make for easier understanding by those coming to know for the first time of the movement of milk in the breast or mammary gland.

We take this opportunity of protesting strongly against the suggestion of Cowie et al.[1] that in lactational physiology the verb "to suckle" should be used for what the baby animal does to get milk from the mamma—and for nothing else. To suckle means (O.E.D.) to "give suck to" and it is in this sense that the word is most

1. Cowie, A. T., Folley, S. J., Cross, B. A., Harris, G. W., Jacobsohn, D., Richardson, K. C. *Nature, Lond.* 1951, **168**, 421.
2. Folley, S. J. *Brit. med. Bull.* 1947, **5**, 142.

commonly (and correctly) used. Rarely (O.E.D.) it is used for what the baby animal does, but to encourage this use would promote confusion, for the correct use, in the sense of what the lactating animal does, will certainly be continued by many writers. Nor is there any possibility at all that writers on lactation would agree to use "to suckle" *only* for what the baby animal does. Agriculturists, we are assured, use the terms sucking pigs and suckling sows. Perhaps the noun "suckling," used of a young animal that is suckled, may be the origin of the confusion, if it has not been recalled that the termination "-ling" is a diminutive (duckling, gosling, princeling); so a suckling is a little thing that sucks, a little sucker.

For what the lactating animal does so that the baby may get milk, Cowie et al. suggest that the term "*nursing*" should be used. This word has, both in common usage and in dictionary definitions, far wider vaguer implications and its use seems to us totally unnecessary, although if it is used in the connotation of what the lactating animal does, it is not likely to lead to such confusion as would the use of "to suckle" for what the baby does.

For what the baby animal does to get milk from the mammary gland, "sucking" or "feeding" or, of humans, "taking the breast" appears to us suitable, although the process is more elaborate than the primary meanings of these words imply, as indeed the discussion at the British Association is sure to show.

Obstetric Hospital, University College Hospital, London, W.C.1. MAVIS GUNTHER.
Guy's Hospital, London, S.E.1. RONALD MAC KEITH.
Cockermouth, Cumberland. CHARLOTTE NAISH.
British Hospital for Mothers and Babies, Woolwich, London, S.E.18. HAROLD WALLER.

BORIC-ACID POISONING

SIR,—I note, in your issue of March 6, an editorial concerning boric-acid poisoning, in which I am quoted.

You say that there is no good reason for including boric acid in dusting-powder. This ignores completely the fact that boric acid is added to talcum powder, not so much for the antiseptic value but for the chemical effect in neutralising the alkalinity due to the 2–6% of calcium oxide in commercial talcs available on the market. In solution when the talc is wetted, boric acid reacts with the calcium hydroxide to produce the highly insoluble calcium borate, thus neutralising this alkalinity and, at the same time, being removed in the process. A small residuum of boric acid present in talc intended for the diaper area provides a desirable buffer action to neutralise any ammoniacal fermentation products occurring in urine, and by this chemical buffer action it discourages the growth of the alkaline ammonia-splitting organisms which are said to cause diaper rash. A third effect of boric acid in the borated talcs is to discourage fungal growth in the product during counter storage.

Regardless of the fact that boric acid can be toxic when misused, it is still true that it is a useful agent in solution for the treatment of many forms of contact dermatitis, and many dermatologists feel it to be a valuable agent in their practice.

McGillivray and Fraser [1] infer that the turmeric and carmine tests for boric acid are adequate to indicate its presence and, therefore, enable the diagnosis of boric-acid poisoning to be made. They overlook completely the excellent work of Kent and McCance [2] and others who have shown that boron is a normal constituent in the diet and hence normal people may be expected to excrete significant quantities of it. Feigl states that the limit of sensitivity of the turmeric test is 1 : 2,500,000. This is approximately 2·4 mg. of boric acid per litre. Dunn and Bloxom [3] report that orange pulp contains from 3·5 to 14 parts per million of boron and, using the higher figure, it is calculated that a 4-ounce intake of orange juice might contain as much as 9·6 mg. of boric acid or 6 times enough boron to produce minimum positive turmeric test assuming 0·75 litre of urine output per day. Thus, the turmeric reaction, while a test for boric acid, actually reveals only the presence of a chemical which is frequently a normal component of urine, and "positive" tests cannot be interpreted to mean poisoning. Quantitative blood-boron analysis is the only chemical procedure of diagnostic value, and the blood-levels which must be demonstrated should be well in excess of 1 mg. per 100 ml. which has been observed to occur, not infrequently, in normal individuals with no signs of toxicity. The acute cases of boric-acid poisoning in our experience usually show in excess of 100 mg. per 100 ml. of boric acid in the tissue. This in itself points out the relatively low toxic potential of this compound.

I do not mean to indicate that boric acid cannot be harmful if misused. The cases I have reported, and others in the literature, including the case of ingestion of borax described in your issue of March 6 by Dr. Living-Taylor, point out the necessity for common sense in its application and the prevention of it being taken by mouth, as in the curiosity poisoning Dr. Living-Taylor reported. Goldbloom and Goldbloom,[4] who are quoted in your article, originally reported a case of boric-acid poisoning from borated talc. This case has subsequently been disproved and the Goldblooms have published [5] a retraction of this allegation.

The Ducey and Williams paper,[6] showing that application to injured skin of a 5% dusting powder can lead to severe poisoning, is not a case-report but a lot of speculation based on the assumption that all of the boric acid present in borated talc would be absorbed if applied to irritated areas. They completely overlooked that the boric acid in such a preparation would not be available for absorption since it would have been removed by the reaction with the alkaline constituents of the talc. Finally, their suggestion that 5 mg. per 100 ml. is the near-lethal concentration of boric acid is not supported by any carefully studied cases in the literature and is contradicted by our personal observations of infants with this blood-level after actual ingestion of boric-acid solution but who showed no significant toxic effects.

In summary, despite the fact that boric acid and borax have caused poisoning, careful study shows no such effects from 5% borated talc. The bona-fide poisoning cases illustrate the common denominator of careless parenteral or oral administration of the drug or the gross misuse of the chemical by frequent application to large areas of irritated skin of small infants. I have warned against the latter, but, in defence of boric acid, I maintain that it is still a very useful compound in dermatological practice and as a home remedy.

RUSSELL S. FISHER
University of Maryland Medical School, Baltimore, Maryland. Chief Medical Examiner, State of Maryland, and Professor of Legal Medicine.

1. McGillivray, P. C., Fraser, M. S. *Arch. Dis. Childh.* 1953, **28**, 484.
2. Kent, N. L., McCance, R. A. *Biochem. J.* 1941, **35**, 837.
3. Dunn, J. T., Bloxom, H. C. L. *Analyst*, 1929, **54**, 28.
4. Goldbloom, R. B., Goldbloom, A. *J. Pediat.* 1953, **43**, 631.
5. *Ibid*, 1954, **44**, 720.
6. Ducey, J., Williams, D. B. *Ibid*, 1953, **43**, 644.
7. Bavin, E. M., Drain, D. J., Seiler, M., Seymour, D. E. *J. Pharm., Lond.* 1952, **4**, 844.

A NEW DERIVATIVE OF ISONIAZID

SIR,—The letters in your issue of Aug. 14 by Dr. Nagley and by Mr. Bavin and his colleagues, on the salicylaldehyde hydrazone derivative of isoniazid (salizid), prompt us to give our experience with this drug. Salizid was synthesised in these laboratories early in 1952 and was then made on a large scale for clinical trial in the United States by the Nepera Chemical Co., New York. We were unaware of the publication of Bavin et al,[7] although we have noted reports from other laboratories of the synthesis of this compound.

A brief mention of our findings with salizid has already appeared,[8] but in view of the more widespread interest now being taken in it, it would perhaps be helpful to relate our experimental findings in greater detail.

In Vitro

In a Proskauer and Beck type medium, salizid and isoniazid both caused complete inhibition of H37Rv for 14 days at a concentration of 0·06 μg. per ml. At the end of 28 days the inhibitory concentrations had increased to 2·0 (salizid) and 13·0 (isoniazid) μg. per ml. Using inocula, prepared from growth in tubes containing the highest concentrations of the respective drugs, for fresh series, it was found that the inhibitory concentrations after 14 days had increased to 0·3 μg. per ml. (isoniazid) and 3·0 μg. per ml. (salizid). From this we concluded that strains resistant to salizid emerge at least as readily as strains resistant to isoniazid.

When tested against an isoniazid-resistant variant of H37Rv, it was found that isoniazid was inhibitory for 14 days at 66 μg. per ml. and salizid at 50 μg. per ml.

In Vivo

The activity of isoniazid and salizid in suppressing intravenous infections in mice were compared, using the Ravenel bovine strain of *Mycobacterium tuberculosis* and an isoniazid-resistant variant of it (resistant to 100 μg. isoniazid per ml.). The results are given in the accompanying table. Treatment was for 14 days (drug in diet) and median survival times of control untreated mice with both strains were approximately 17 days.

Ravenel Rv (isoniazid-sensitive)		Ravenel Rv (isoniazid-resistant)	
Daily drug intake (mg. per kg.)	Change in ST_{50} in days	Daily drug intake (mg. per kg.)	Change in ST_{50} in days
Isoniazid 6·4	+ 9·0	Isoniazid 28	+1·0
Isoniazid 25	+150·0	Isoniazid 42	+1·5
		Isoniazid 114	−1·0
Salizid 9·25	+ 0·5	Salizid 21	−2·0
Salizid 48·0	+157·0	Salizid 46	+0·5

A combination of equal parts of isoniazid and salizid was completely ineffective at a dose of 96 mg. per kg. in mice infected with the isoniazid-resistant variant.

These findings suggest that while salizid may be useful in the clinic as an alternative to isoniazid, it holds no promise as an adjuvant to isoniazid nor for treatment of cases where strains of *M. tuberculosis* resistant to isoniazid have developed.

Laboratories of the Medical Research Council of Ireland, Dublin.

VINCENT C. BARRY
MICHAEL L. CONALTY.

YOUNG RECRUITS TO NURSING

SIR,—While it is most necessary to look to ideals as regards nursing recruitment, it is very worrying to face daily the realities of the problem of supplying hands to perform the nursing acts, and then to read your complacent annotation of Aug. 14.

The General Nursing Council are solely concerned with the training of nurses and have no responsibility as regards staffing of hospitals; they therefore can rightly look for ideals. The hospitals and their management committees are concerned with the problem of nursing the patients already in the beds and are faced with reality. There are not enough nurses. Will increasing the age-limit of entry obtain more? Surely the task is to fill the ranks and then start to prune.

The comparison with the old child labour problem is hardly fair unless all industry is included. Girls of 16 years and upwards are employed in industry today, many doing strenuous jobs. Why should they not enter nursing at the same age? Girls of 16 years are capable of being mothers. Are many not capable of looking after sick children? That there is undoubtedly a grim side to nursing is stressed rightly in your article, but on the other hand a children's unit can be an ideal training ground to prepare a girl for her future career, and indeed for motherhood.

A girl who enters her chosen profession on leaving school stands a much better chance of settling down than her colleague who spends the first two or three years in other employment. The latter will think twice about giving up industrial hours to the more spread-over hours of nursing. It is a fact that cannot be stated too often that people are unfortunately sick outside office hours and expect trained nurses to be waiting to look after them.

Nursing orderlies and nursing aides are playing an ever-increasing part in the work of the modern hospital, but it must be remembered that because of shortages they are in some instances bearing responsibilities which, however capable they are, they should not be called upon to hold. There must be at all times an adequately trained staff to guide them. Part-time nurses, who have responded to appeals for assistance, also help; but in many instances they inadvertently cause trouble because they work at *their* times—which, because they have other commitments, often exclude night duty and weekends. There are also frequent financial comparisons which do not help for unity.

There must be a change of outlook towards nursing. One so often hears ill-considered statements such as "I would not let my daughter take up nursing." It must of necessity be a campaign at a national level—it is a national problem—and it is unfair to blame management committees and hospitals if there is lack of personnel available. Hospitals are in dire need of nursing staff, and it would be interesting to learn what are the "better ways" of obtaining them as suggested in your last sentence. Surely if there is a solution it is long overdue for disclosure.

We need more nurses and some drastic measures are required. Women are always looking for equality. Why should they evade conscription? Many who at present have no idea of the nursing way of life would find enjoyment in the work and stay to complete their training.

My ideal is to see the nursing profession back again in the rightful position it held years ago but with modern amenities and salaries: a profession whose work is carried out for the love of the job and not where the nurse is so harassed that it is impossible to achieve the perfection which leads to satisfaction.

Birmingham. F. L. KER.

"HYPERSENSITIVITY" TO SUXAMETHONIUM

SIR,—It is not surprising that Dr. Calvert and his colleagues (Aug. 21) found a test dose of 10 mg. of suxamethonium chloride ineffective in detecting "hypersensitivity" to that drug. For, in fact, their patient, like others with low pseudocholinesterase levels, exhibited not "hypersensitivity" (which implies a reaction to an unusually small dose of drug) but slow recovery following a normal reaction to a normal dose, which is another matter.

von Dardel and Thesleff [1] and Thesleff [2] observed considerable variations in duration of paralysis in different patients from the same dose of suxamethonium per unit of body-weight. It has since been established that such variations correspond to variations in the level of pseudocholinesterase. Thesleff [2] also showed that in a given individual the duration of paralysis increased with increasing dose. These facts are now confirmed once again by Dr. Calvert and his colleagues.

It becomes increasingly clear that the duration of the paralysis depends mainly, if not entirely, upon two factors: (1) size of dose; and (2) level of pseudocholinesterase. Since, at the moment of injecting suxamethonium, the second of these factors is usually unknown

8. Conalty, M. L. *Irish J. med. Sci.* 1953, p. 267.

1. von Dardel, O., Thesleff, S. *Nord. med.* 1951, **46**, 1308.
2. Thesleff, S. *Acta physiol. scand.* 1952, **25**, 348.

I agree that the initial dose should be the smallest that can be counted upon to produce the desired effect. It is an advantage, moreover, to employ this initial dose as a test not of the patient's sensitivity but of his speed of recovery—that is, of his pseudocholinesterase level.[3] Dr. Calvert and his colleagues suggest the range 30–50 mg. for this initial dose but they do not relate it to the patient's weight. In several thousand administrations of this drug I have found weight a valuable guide, and I have suggested [4] the range 0·5–1·0 ml. of 'Scoline' per 100 lb. This gives a more precise guidance than does theirs and, unlike theirs, is applicable to small children and to heavy adults. In electroconvulsive therapy, I have found the lower of my limits consistently satisfactory.

I cannot altogether agree with their opening statement that prolonged apnœa after suxamethonium is rare. I reported its occurrence in 15 out of 1000 patients. In 10 of these the pseudocholinesterase level was estimated and found to be below (in 8) or near (in 2) the lower limit of normal.[4] This, indeed, is approximately the incidence that would be expected from the definition of normal limits.[5] In all these patients the initial dose was within the range mentioned and in only 2 did apnœa exceed 15 minutes. The longest apnœa I have so far encountered was 31 minutes. This patient, who weighed 100 lb. and received 1 ml. of scoline, had the exceptionally low pseudocholinesterase level of 7 units (normal 51–128 units).

St. Thomas's Hospital, London, S.E.1. J. G. BOURNE.

THERAPEUTIC TRIALS

SIR,—The success of therapeutic trials organised by the Medical Research Council has shown the great value of sharing such studies, particularly where the disease concerned is relatively uncommon. So many methods of treatment are constantly being evolved that it is of course impossible for an official body to deal with any but a few of the more immediate problems. As a result much is left to the independent worker, who may waste much time on trials which cannot be brought to a valid conclusion through lack of clinical material. In addition to new remedies there are many older methods of treatment whose power, whether for good or ill, has never been adequately determined and could with advantage be put to the test by modern methods of assay.

I should be glad to hear from any of your readers who would be interested to form a trial group with a view to giving mutual assistance in the solution of such problems, as and when they arise.

Walkden Clinic, Manchester. J. STEWART LAWRENCE.

THERAPEUTIC SOCIAL CLUBS

SIR,—Arising out of recent correspondence in your columns on mental health, may I draw the attention of psychiatrists and general practitioners to the facilities offered by therapeutic social clubs.

The Institute of Social Psychiatry administers a series of these clubs in the London area. They are designed for those convalescing from mental breakdown and for those showing signs of incipient mental disorder, assisting them in social rehabilitation.

The clubs are financed from public-authority grants and from voluntary contributions. Each club is under the supervision of a psychiatrist and trained social therapists. Suitable cases may be enrolled at any time and no membership fee is charged.

The Institute of Social Psychiatry, London, N.W.3. R. A. STEWART
Assistant Medical Director.

3. Bourne, J. G. *Lancet*, 1952, ii, 290.
4. Bourne, J. G. *Brit. J. Anæsth.* 1953, **25**, 116.
5. Callaway, S., Davies, D. R., Rutland, J. P. *Brit. med. J.* 1951, ii, 812.

THE PLACE OF PSYCHIATRY IN MEDICAL EDUCATION

SIR,—I think the most important point Dr. Borg makes in his letter of Aug. 28 is that "for too long psychiatry has developed in isolation away from the main stream of medical advance." I think that it is this isolation that has caused psychiatry to be neglected in the medical curriculum of some schools. To overcome this there should be greater integration; many large teaching hospitals have no psychiatric wards and very few have psychiatrists who regularly visit general medical and surgical wards, and lecture or discuss cases with students in clinical hours.

Dr. Borg suggests a pruning of the preclinical subjects. I do not agree: add a subject—psychology. Who would consider teaching a student medicine or surgery if he had never studied physiology or anatomy? Integrate zoology and botany into a biology course, and add a course in psychology which stresses normal behaviour patterns seen from birth to the grave; later give a course in psychiatry, followed by a professional examination.

Dr. Borg states that psychiatric hospitals are excluded from the list of recognised hospitals for the pre-registration year; this is not so in Scotland where there are quite a number of preregistration posts in mental hospitals.

In the last twenty years there has been a greater understanding of psychiatric problems and I feel we are on the eve of great discoveries; for too long general medicine has developed in isolation away from the main stream of psychiatric advances.

Edinburgh. G. I. SLATER.

TREATMENT OF PLANTAR WARTS

SIR,—I think it is rather unfortunate that the article by Dr. Crow and Dr. Scott (Aug. 14) has given the impression that carbon-dioxide snow is the absolute answer to plantar warts. The technique of freezing described is undoubtedly effective, but it is too brutal to enjoy more than temporary favour. All patients subjected to it complain of severe pain and most consider it agonising.

On the whole parents prefer to have their children treated more comfortably if more leisurely by painting with podophyllin or trichloracetic acid and occluding with 'Elastoplast'; but for the odd patient who wants a quick result I cannot think that anyone with experience in the use of both liquid nitrogen and carbon-dioxide snow would ever prefer the latter. Liquid nitrogen is far more effective and needs to be applied for less than half the time.

Royal Infirmary of Edinburgh. R. M. FOSTER.

CROSS-INFECTION AND THE OILING OF FLOORS

SIR,—We should like to deal with some of the criticisms by Dr. Marsh and Miss Rodway (Aug. 14) of the paper by our colleagues and ourselves.

They say that our test and control periods are not comparable, but do not say why. Inequality of length is no obstacle to comparability, and the lengths of the periods were sufficient to establish satisfactory approximations to the true incidence of cross-infections. Thus, in the control (unoiled) ward, the over-all relative frequencies of nasal cross-infection for the two periods agree closely, in spite of fluctuations from month to month (table IV). The average figures for wounds in the two periods in this ward also agree well (table V).

Dr. Marsh and Miss Rodway imply that our methods of suppressing dust were inefficient and resulted in only a "slight" reduction in colony counts. We used the methods recommended by the Medical Research Council's committee.[1] The reduction in colony-counts was more

1. M.R.C. Committee on Hospital Cross-infection. M.R.C. memorandum no. 11, 1951.

than "slight." As we stated, the slit-sampler counts during the making of unoiled beds were up to 7 times as great, and on the average $3^1/_2$ times as great, as with oiled beds. The increase of count with the making of oiled beds was small, and could not have been much less if we had treated the stuffing of pillows and mattresses. At other times of the day, the average slit-sampler counts in ward 1 were less than half, and during the last three months were less than a third of the average counts before oiling. Our settle plates were exposed for two hours, although this period sometimes gave an overcrowded growth, in order to obtain reasonable numbers of *Staphylococcus aureus* colonies for counting. The overcrowding may have reduced the difference between the total counts of the control and test-period plates, but in spite of this the average number of *Staph. aureus* colonies after oiling was less than before oiling by about 60%. This is more than a slight reduction.

We did not expect to abolish dust completely, since it comes from other things besides bedding. We do not think that the reduction of dust-borne bacteria would have been much greater if we had oiled ledges, table tops, lockers, door architraves, and shelves. The combined area of these surfaces is much less than that of the floor, and throughout the hospital they are cleaned by wiping with oil-impregnated dusters. Dr. Marsh and Miss Rodway say that we did not oil screens or curtains. We did oil screens, and said so. There were no curtains in the wards.

Since we could detect no significant reduction in cross-infection rates in spite of a substantial reduction of aerial contamination, we concluded that dust, or at any rate bedclothes dust, played at most a minor part in the transfer of staphylococcal infection from person to person in our ward. When we stated our belief that spread by contact may be the most important mode of dissemination of resistant staphylococci in surgical wards, we meant important in causing the infections with which our paper was concerned. We cannot see why we should have concluded from our findings that the staphylococci on settle plates got there by contact.

SUZANNE K. R. CLARKE
Bristol Royal Infirmary. W. A. GILLESPIE.

PERIPHERAL NEUROPATHIES WITHOUT ANÆMIA

SIR,—We were interested to read the paper by Dr. Jewesbury in your issue of Aug. 14, for we have a case in the ward at the moment similar to those he reported.

A 41-year-old housewife complained of tiredness for a year, and aching pains and numb feelings in the legs for five months. The pain radiated down the legs to the calves and was worse in bed at night, keeping her awake. She also had numb feelings and pins-and-needles in the hands for a similar period. Her appetite had been poor and she had lost a stone in weight in the past year. Her menstrual periods were regular but scanty. One brother had died from pernicious anæmia fifteen years ago.

She looked pale and her teeth were carious, but there were no abnormal physical signs in the cardiovascular and respiratory systems. The calves were tender and there was diminished sensation to pinprick over the lower legs and loss of vibration sense in the malleoli. Hb 86%, red cells 4,150,000 per c.mm., colour-index 1. Fractional test-meal showed a histamine-fast achlorhydria.

She was given vitamin B_{12}, 100 μg. intramuscularly on alternate days, and within ten days her symptoms had subsided. She felt better and the calves were less tender, but there has been no change in sensory loss up to date.

Unfortunately a sternal puncture was not performed, but her response to vitamin B_{12} was convincing enough for us to consider that this case may well be an example of Dr. Jewesbury's "vitamin-B_{12} deficiency."

The Royal Free Hospital, North Western Branch, Hampstead, London, N.W.3. E. V. HESS
F. CLIFFORD ROSE.

DETERMINATION OF URINARY 17-KETOGENIC STEROIDS

SIR,—In your issue of Aug. 21 Mr. Norymberski and Mr. Stubbs drew attention to your leading article of July 3 in which a report by Brooks and Clayton [1] to the Society for Endocrinology was quoted. Brooks and Clayton, adapting the M.R.C.[2] method for the estimation of 17-ketosteroids to the method of Norymberski and his colleagues for the estimation of 17-ketogenic steroids, were unable to obtain satisfactory recoveries of hydrocortisone and cortisone. In their letter, Mr. Norymberski and Mr. Stubbs show very elegantly that the success of the former's method depends to a surprising extent on the use of ethylene dichloride as the extracting solvent. One of us (R. V. B.) has indeed been able to obtain recoveries of 96% of hydrocortisone added to urine, using ethylene dichloride for extraction. We would hasten to agree that the poor recoveries obtained by Brooks and Clayton do not in fact reflect on the reliability of the method for 17-ketogenic steroids proposed by Norymberski et al.,[3] but they underline the necessity for careful attention to the nature of solvent mixtures used in steroid analysis.

R. V. BROOKS
Department of Chemical Pathology, St. Thomas's Hospital Medical School, London, S.E.1. BARBARA E. CLAYTON
F. T. G. PRUNTY.

ÆTIOLOGY OF ECLAMPSIA

SIR,—Your issue of July 31 contains material of the utmost importance to the obstetrician, for it includes two of the most valuable contributions made to his knowledge in recent years. You are heartily to be congratulated on it.

Dr. Byrom demonstrates that ischæmia *passively* imposed on the kidney by the Goldblatt clamp is responsible for encephalopathy when the hypertension it provokes is much increased. He has further shown that immediate and dramatic recovery follows restoration of the renal blood-flow. Thereby he offers convincing proof that renal ischæmia can largely explain the toxæmia observed clinically, and it may be inferred that therapeutic agents that reduce renal resistance owe their value to this action. His data also go a long way to confirm the renal-ischæmia hypothesis advanced by Gaunt and Renzi [4] to explain the more complete eclampsia-like syndrome that renin provokes in rats primed with salt and deoxycortone, referred to in a letter by Dr. Corcoran—the second important contribution on this subject in the same issue.

Gaunt and Renzi's experiments also provided a parallel effect to the removal of the Goldblatt clamp when hydrazinophthalazine ('Apresoline') was administered half-way through the interrupted exhibition of renin, for this substance caused immediate and dramatic recovery of the experimental animals and completely protected them from the otherwise vasculotoxic effects on kidney and brain.

Those who study Dr. Byrom's paper must be greatly impressed by the fact that the substitution of saline solution for drinking-water in these experiments accelerated the cerebral attacks and that *some animals so treated had sudden generalised œdema*. Severe renal ischæmia thus *passively* effected, by the clamp, produced the major—and also the rarer—symptoms of eclampsia but failed to cause albuminuria or renal damage. On the other hand, a very severe renal ischæmia, *actively* evoked, as in the Gaunt and Renzi experiments, included these effects. Dr. Byrom ascribes the absence of these renal vasculotoxic changes in the single kidney to its

1. Brooks, R. V., Clayton, B. E. Communication to the Society for Endocrinology, June 11, 1954.
2. M.R.C. Committee on Clinical Endocrinology. *Lancet*, 1951, ii, 585.
3. Norymberski, J. K., Stubbs, R. D., West, H. F. *Ibid*, 1953, i, 1276.
4. Gaunt, R., Renzi, A. A. *Amer. J. Physiol.* 1953, **175**, 313.

protection from the severe hypertension which the clamp imposes.

As renin has been shown by Daniel et al.[5] to produce an active renal cortical shut-down, it would be reasonable to assume that, in Gaunt and Renzi's experiment, such a process operated and that the intralobular artery and its branches, at least in its distal extent, were under pressor influence and thereby aggravated the intrarenal hypertension permitting vasculotoxic changes, and brought the symptoms into line with those in the severer grades of eclampsia. Hæmodynamics of such a pattern are characteristic of the Trueta mechanism and are the basis of toxæmia in man. The noxious influence of salt in both sets of experiments, which is met with clinically, further supports this thesis.

Dr. Corcoran advances the matter. He claims that the vasculotoxic property is intrinsic in renin action. (Provided, presumably, that the ischæmic kidney is not protected against hypertension, it would always display this effect.) He also suggests "an appropriate abnormal balance between altered renal circulation and residual tubular tissue" as a cause of hypertension in pyelonephritis—a design that the pattern of the Trueta renal diversion embraces. Still more significant is his statement that the renin-angiotonin system, known to produce renal ischæmia, is also capable of reducing tubular reabsorption of water, thereby signifying the interdependence of tubular and glomerular function. The publication of his data will be eagerly awaited for any hæmodynamic explanation it may offer for this phenomenon.

Experimentally, small doses of renin have a slight antidiuretic effect,[6] and in dogs it appears to produce a considerable antidiuresis.[7] Yet renin is generally held to cause a diuresis. Gaunt and Renzi's experiment in the primed rat evoked an antidiuresis—bringing its effect into line with the toxæmic symptoms. But Dr. Corcoran's results show a diuresis in certain cases, and provide an analogy with this clinical manifestation in chronic hypertension.

One small amplification is needed in the explanation of decreased filtration fraction in acute glomerulonephritis, in addition to the probable reduction in functional glomerular surface that Dr. Corcoran mentions: that is the existence of an increased plasma-flow revealed by extraction determinations of *p*-amino-hippuric acid[8]—a fact that could easily support a diversion of renal blood-flow of the Oxford pattern.[9]

The positive evidence given by Dr. Byrom and Dr. Corcoran goes far to demonstrate that renal ischæmia is a fundamental cause of eclampsia and pre-eclampsia, and that re-establishing the renal blood-flow is imperative in treatment, possibly because the revascularised kidney is once again enabled to destroy the pressor substances it helped to create when it was ischæmic.[10]

London, W.1. JOHN SOPHIAN.

ACUTE APPENDICITIS: A HISTORICAL SURVEY

SIR,—After Mr. Shepherd's article (Aug. 14), it might not be without interest to note that Charles Darwin [11] gave two references [12 13] in which death from appendicitis is attributed to "small hard bodies, such as seeds entering the passage and causing inflammation."

London, N.W.11. I. GOTTLIEB.

5. Daniel, P. M., Prichard, M. M. L., Ward-McQuaid, J. N. *J. Physiol.* 1954, **124**, 106.
6. Smith, H. W. The Kidney. New York, 1951.
7. Whitney, J., Smith, S., Marmotson, J., Goodman, H., Sellers, A. *Amer. J. Physiol.* 1954, **176**, 419.
8. Bradley, S. E., Bradley, G. P., Tyson, C. J., Curry, J. J., Blake, W. D. *Amer. J. Med.* 1950, **9**, 772.
9. Sophian, J. Toxæmias of Pregnancy. London, 1953; pp. 41, 42.
10. Grollman, A., Muirhead, E. E., Vanatta, J. *Amer. J. Physiol.* 1949, **157**, 21.
11. Darwin, Charles. The Descent of Man. London, 1922 (reprint of 2nd edition, 1874); pp. 29, 30.
12. Martins, M. C. De l'unité organique: in *Revue des Deux Mondes*, June 15, 1862, p. 16.
13. Hackel, E. Generelle Morphologie. Vol. ii, p. 278.

FALSE READINGS OF E.S.R.

SIR,—It may interest doctors who occasionally measure erythrocyte-sedimentation rates using the Westergren technique that the use of 3·8% sodium citrate solution containing 0·2% chlorocresol, as prepared by certain pharmaceutical firms and intended for therapeutic intravenous use, may produce significantly false readings.

Following the inadvertent use of such a solution, it was observed that slight hæmolysis occurred and that sedimentation was in some cases appreciably retarded. When 0·2% *w/v* chlorocresol was added to a portion of a freshly prepared 3·8% citrate solution, only the duplicate tubes using the contaminated solution showed this phenomenon.

Canadian Red Cross Memorial Hospital, Taplow, Berkshire. S. C. MILAZZO.

PROSTATIC CARCINOMA AND MACROCYTIC ANÆMIA

SIR,—In your leading article of July 10 you comment on the possible links between cancer and other metabolic processes. It is probably worth while drawing attention to a case of prostatic carcinoma in which, two years after the onset of urinary symptoms, a macrocytic anæmia developed. The significant feature of the case is that with vitamin-B_{12} therapy not only did the anæmia rapidly resolve, but at the same time there was complete remission of all urinary symptoms which by then had become almost unbearably troublesome.

The patient, now aged 83, began to suffer, early in 1950, from symptoms suggestive of prostatic obstruction. The urologist's diagnosis of prostatic carcinoma would appear to have been confirmed by the spectacular response to diencestrol therapy.

Early in 1952, in spite of continuing treatment and in the absence of any detectable urinary infection, frequency returned and became progressively worse, reaching 20–30 times in 24 hours. At about the same time, he was noticed to have a progressive anæmia which did not respond to iron. This was assumed to be cachectic and terminal. Further investigation proved it to be macrocytic, and both anæmia and urinary symptoms disappeared in dramatic fashion soon after starting vitamin B_{12}.

His improvement has been maintained and confirmed by urologist and hæmatologist. The patient claims that he has never felt better in his life and that he never needs to rise more than once nightly. For obvious reasons there was no histological proof of malignancy and no metastases could be discovered by X-ray examination. Furthermore, because of his age and because he was investigated as an outpatient, no bone-marrow biopsy was carried out. Nevertheless, the results of therapy seem to support the diagnosis of prostatic carcinoma and a concurrent pernicious anæmia.

It is known, of course, that spontaneous and protracted remissions may occur in cancer, and it is also possible that successful treatment of the anæmia in this case may have boosted a natural resistance to the growth. Nevertheless, in view of the concluding remarks in your leading article, I report this as an interesting and relevant case, because:

(1) Pernicious anæmia has its associated neuropathy and a direct association with gastric carcinoma.

(2) There is reason to suppose that there are some unknown factors interfering with hæmoglobin synthesis and red-cell formation in the presence of certain neoplasms.[1]

(3) Animal experiment has suggested that vitamin B_{12} might be effective in the treatment of some cases of malignant disease, and it has recently been reported [2] that several cases of neuroblastoma have shown remarkable and lengthy regression after treatment with vitamin B_{12}.

Edinburgh, 9. S. LIPETZ.

1. Homburger, F., Fishman, W. H. The Physiopathology of Cancer. London, 1953.
2. British Empire Cancer Campaign. 31st annual report, 1953.

PREPARATION OF BLOOD-FILMS IN SUSPECTED MALARIA

SIR,—In your issue of July 10 (p. 97) reference was made to the large number of cases of malaria which have been reported in this country during recent years, chiefly among members of H.M. Forces returning from Korea, Hong-Kong, and Malaya. General practitioners were warned that such cases might act as foci for outbreaks of indigenous malaria, and stress was laid on the importance of making blood-films from all suspected cases.

The following notes on the technique for preparing such films may be found helpful.

Slides

If possible, these should be new ones. Scratched or foggy slides should never be used. Before making blood-films, the slides should be taken through an ether alcohol solution, equal parts, and wiped with a clean, dry cloth. Unless the *slides are quite free from grease, thin blood-films will not* spread evenly and thick drops will peel off during the process of staining.

Thin Films

After cleaning the pad of the finger or lobe of the ear, *the skin should be wiped dry. Puncture the skin with a straight* triangular surgical needle and wipe off the first drop of blood. A bead of blood for a thin film should be no larger than the head of a pin. If a slide is used for spreading a film, see that it is a thin one and has a smooth edge. Contact of the slide with the bead of blood should be at an angle of 45° and the film should be made by pushing away from the blood. The aim in making a thin film should be to have the corpuscles *only one deep; the cells should almost touch one another* but not overlap. Good thin films cannot be made if a thick slide is used for spreading the film or if the drop of blood is *too large.*

Thick Films

A large drop of blood is placed in the centre of a clean slide and then distributed in a circular movement with the edge of another slide. The correct thickness of a thick film can be determined in the following way. After distributing the blood, place the slide over a piece of newspaper or over the face of a watch. The small print or the hands of a watch should only just be visible. If these cannot be seen the drop is too thick and if seen too clearly, it is too thin. After preparing a thick *film, lay it flat until it is quite dry. If flies are about, films* should be covered with a Petri dish, otherwise the blood will be eaten by them.

Films, when quite dry, should be wrapped in tissue paper and securely packed. One thin and one thick film (unstained) should be sent, but preferably two of each. Blood-films, preferably unstained, may be sent to the Medical Research Council Malaria Reference Laboratory, Horton Hospital, Epsom, Surrey.

Malaria Reference Laboratory, Epsom, Surrey. P. G. SHUTE, Assistant Director.

FINGER CLUBBING

SIR,—Dr. Pyke's assessment, in his article of Aug. 21, of the validity of finger clubbing as a physical sign is valuable additional evidence of invididual fallibility, and leads to similar conclusions to those drawn from comparisons of such things as the interpretation of radiographs.

There appears, however, to be a fallacy inherent in his material. He states that only 4 observers (the students) used the nail-bed angle as their criterion, while all 12 doctors used other evidence. This seems to imply that the outline of the finger-tip was considered by them to be of some importance. Yet the method employed to photograph the fingers is very ill designed to reveal outline. The fingers are lit almost axially, thus leaving the edges of the outline in deep shadow, and they are placed against a dark, almost black, ground. In the half-tone reproductions at least, it is impossible to make out the outline.

I suggest that in these and similar cases, where outline is significant, the surface lighting is chosen appropriately to the subject, but the background is transilluminated, so that the image has no external shadows whatever. The procedure is simple, calling only *for an X-ray illuminator, and a few simple tests will* indicate the correct light balance and exposure factors. The example in the accompanying photograph is of a rather gross case, but it indicates the accurate delineation of outline which is possible. The method, I would add, is well known to all experienced medical photographers.

Department of Medical Illustration, Manchester Royal Infirmary. ROBERT OLLERENSHAW.

HISTORY OF INGUINAL-HERNIA REPAIR

SIR,—Reading one of your leading articles [1] of 1951 has encouraged me to write about several points in the history of inguinal-hernia repair about which there appears to be widespread confusion. These are: (1) the *relaxation incision in the sheath of the rectus muscle;* (2) the operation utilising the rectus muscle itself to reinforce the Hesselbach triangle area ("pubic corner"); and (3) the use of a flap of the external sheath of the rectus to reinforce the same area.

The relaxation incision in the sheath of the rectus muscle was, so far as I have been able to find out, first used by Halsted and was described by him in 1903.[1] The relaxation occasioned by this incision generally allows the conjoined tendon to be brought down to *Poupart's ligament without tension. The method* was reported by Halsted in a moderately long article on *inguinal-hernia repair, and for this reason was probably* overlooked by a great many subsequent workers in this field. Fallis,[2] Rienhoff,[3] and Tanner [4] much later published what is very much the same method. I believe that in England the method is generally known as the "*Tanner slide.*"

Cases which often give a great deal of trouble are those in which there is a paucity of tissues for closing the "critical angle" in the pubic corner at the lower end of the inguinal canal. The trouble here is often that there is either no conjoined tendon, or the conjoined tendon, instead of being attached to the spine of the pubis, is attached higher up to the linea semilunaris. This leaves a triangular area in which there is a tissue defect. In order to close the area in the usual fashion, poor structures would have to be sutured together under considerable tension. In order to obviate this, Bloodgood [5] split the posterior border of the lateral edge of the sheath of the rectus and brought the muscle-fibres of the rectus muscle itself down to Poupart's ligament, suturing them there and thus closing the area. Wölfler [6] had used a similar method before Bloodgood. Halsted [7] states that Bloodgood knew nothing of Wölfler's operation at the time he first used his own method, and that Wölfler

1. Halsted, W. S. *Bull. Johns Hopk. Hosp.* 1903, **14**, 208.
2. Fallis, L. S. *Ann. Surg.* 1938, **107**, 572.
3. Rienhoff, W. F. jun. *Surgery*, 1940, **8**, 326.
4. Tanner, N. C. *Brit. J. Surg.* 1942, **29**, 285.
5. Bloodgood, J. C. *Johns Hopk. Hosp. Rep.* 1899, **7**, 232.
6. Wölfler, A. *Beitr. Chir.* 1892, p. 552.
7. Halsted, W. S. Surgical Papers. Baltimore, 1924; vol. 1, p. 306.

antedated Bloodgood in the actual use of the method by only a few months. Wölfler's method was different anyway in that he used the rectus muscle itself to strengthen the entire length of the inguinal canal, instead of just the lower critical angle, as was the case with Bloodgood.

The use of a flap of rectus sheath to close the lower critical angle or pubic corner is often incorrectly attributed to Bloodgood. Perusal of his papers, however, will show that is not correct. Halsted [1] first used it in this country, and his method was published at the same time as his relaxation incision in the sheath of the rectus muscle. But Berger [8] had preceded Halsted in the use of a flap of rectus sheath to repair an inguinal hernia. Here again, however, he did not use the flap in the same way, but used it to reinforce the entire length of the inguinal canal instead of just the lower critical angle. Again, Halsted [7] also knew nothing of Berger's operation at the time his own operation was published.

While these points may be of academic interest only, they will probably be of some value to the historically minded surgeon.

Baltimore. AMOS R. KOONTZ.

PHYSIOTHERAPY IN THE HOME

SIR,—Though I am 75, I have never had to trouble a doctor since my two children were born. Last winter I started to have painful rheumatism in my knee, which I attributed to old age. I rubbed it with a medicated oil—without much relief. A few months ago I bought an old-fashioned rocking-chair in which I sit for a couple of hours each day, gently rocking myself, while listening to the wireless. Recently I have noticed that this rocking gently exercises the muscles from hips to feet—which perhaps explains why I can now kneel comfortably, run up stairs, and do my own housework.

For old people, this form of exercise has the advantage that it tires neither heart nor feet.

Worthing. M. STANGER.

Medicine and the Law

THE LAW AND THE HOMOSEXUAL

FROM A CORRESPONDENT

EUROPEAN legal codes, notably those of the Scandinavian countries and of France, differ fundamentally from our own in their treatment of homosexuals. The Home Secretary's committee, appointed in July to inquire into the law relating to homosexual offences and prostitution in this country, has not been asked to study the position in foreign countries, but the experience and practice of these countries ought to be taken into account. Laws are part of the social system in which they have developed and what is successful in one country is not necessarily successful in another. But when we are reconsidering a problem it seems sensible to draw not only on our own national experience, but also on that of other countries; to pick here and there from what seems most effective in their practice.

The laws and practice of other countries show considerable diversity, but the English law and English courts have few rivals in their severity towards homosexual conduct among adults. As the law of this country stands, homosexual conduct among men is, without exception, a serious criminal offence. The maximum penalty, under certain conditions, may be imprisonment for life. Prosecutions for unnatural offences and indecency between males, including attempts at solicitation, are common and their number has increased substantially since the war. A term of imprisonment is still the penalty inflicted in about half the cases found guilty. Answers to parliamentary questions suggest that few of these men receive systematic psychiatric treatment in prison, though more than five years ago a joint committee of the Magistrates' Association and the British Medical Association affirmed that

"punishment without treatment is not likely to have beneficial effect; indeed it can make these offenders worse and thus more likely to repeat their offences."

THE CHARGE

Under some Continental systems homosexual activities are not a criminal offence. It is held to be neither desirable nor possible for the law to control misbehaviour which is practised in private without demonstrable harm to the community at large. According to the criminal code of Denmark of 1930, which may be taken as typical of the modern Scandinavian attitude to this problem, male homosexual intercourse is a punishable offence only where one of the partners is under 18 years of age, or where payment is received. It is not an offence to offer to give payment. Otherwise homosexual conduct is not in itself held to be a crime though it may, of course, be punished on other grounds, such as public indecency.

The French code of criminal law is equally clear-cut. Until 1942 French law did not recognise homosexuality itself as a crime. Homosexual conduct can, of course, lead to another criminal offence; thus sexual intercourse among males is punishable if committed in public because it is an act of public indecency; if it involves minors under the age of consent (15 years); if it is accompanied by physical violence; or if it takes the form of incitement to prostitution. Even today homosexual intercourse in private among consenting adults is not an offence in France, but in 1942 an ordinance was introduced making unnatural practices among males punishable by six months to three years' imprisonment and a maximum fine of £1000 where one of the partners is under the age of 21. The French courts have dealt severely with cases brought under this ordinance.

These are all examples of the specific circumstances in which the criminal courts of some European countries will institute prosecutions for homosexual acts. Together they probably cover the chief exceptions which would have to be made even if punishment for homosexual conduct between consenting adults were to be abolished—namely:

(*a*) If it is committed in a public place or place of public resort.
(*b*) If one of the partners is under the age of consent.
(*c*) Where physical force is used or improper pressure brought to bear.
(*d*) Where payment or prostitution is involved.
(*e*) Where enlisted men in the Armed Forces are concerned.

Soliciting in public places, at present punishable under English law as an attempted homosexual offence, is a separate problem, for it is a public nuisance. Here a possible change to be considered is that prosecutions should no longer be brought by the police but only on the complaint of the person approached, except where minors are concerned.

THE SENTENCE

Whether criminal law should concern itself with homosexual relations conducted in private by consenting adults is not the only question where comparisons with foreign legal codes may prove useful. Almost equally important is the courts' approach to the task of imposing sentence on offenders whose guilt has been established. Here experience and experiments in the United States may repay investigation.

The statutes of the different American States which deal with homosexuality completely lack uniformity. Retribution ranges from the threat of life-sentences in three States to fines in six others and complete immunity in New Hampshire and Vermont. Indeed within the

8. Berger, P. *Rev. Chir.* 1902, **25**, 1.

United States legislation for this offence varies more widely than between all the nations of the world. But in some States (and, incidentally, also in Canada) efforts are being made to secure for the courts the help of a qualified medical practitioner before sentence is imposed on a sexual delinquent. Minnesota, Wisconsin, and the District of Columbia already have laws which provide for the compulsory examination by qualified psychiatrists, appointed by the court, of any person, who, at his trial, is suspected of being a sexual psychopath. In Minnesota if the diagnosis is confirmed the accused man or woman cannot be sent to prison, but must be confined at a psychotherapeutic centre or a hospital.

Under English law criminal courts have no power to nominate experts to examine the accused. But, provided the offender is willing to coöperate, magistrates' courts as well as quarter sessions and assizes may make a probation order requiring him to accept medical treatment. These powers were widened by the Criminal Justice Act of 1948.

In Western Germany, where unnatural offences and indecency among males are still punishable by sentences of up to five years, though prosecutions except for aggravated offences are today uncommon, lawyers and doctors have lately asked that where there is hope that treatment may be effective, the offender should be put on probation rather than in prison.

Aftercare of sexual offenders can perhaps best be studied in Scandinavia where a good number of experiments are under way, including the Herstedvestor Institution. In Denmark [1] selected prisoners who accept castration are released. In the last twenty years some 300 people have been castrated and some 2000 sterilised.

Public Health

Tuberculosis Morbidity

IN the medical-text volume of his Statistical Review for 1950, published last week,[2] the Registrar-General examines the evidence for and against a decline in morbidity from tuberculosis, as an accompaniment to the reduction in mortality since 1947. Notification-rates in 1950 are compared with those for earlier years. Mass radiography, improved chest-clinic facilities, and a better public attitude to the disease have so increased the efficiency of case-finding that notification-rates for the years following the late war are not really comparable with those of earlier years. It is even doubtful whether, as the rates at first suggest, the incidence of new cases is higher in 1950 than it was in 1938; but it is more certain that the reduction in rates at most ages in the last two or three years is a real one. During the late war the notification-rates for respiratory tuberculosis rose in both sexes in the most vulnerable age-group (15–24). Among males there has been much improvement from the peak of 1948, and, when allowance is made for better detection, it seems likely that the morbidity in this age-group had reverted to pre-war level by 1950. Among young women, however, the figures suggest that the war-time rise in morbidity from respiratory tuberculosis persisted up to 1950. The experience of other age-groups has been different, but there is enough evidence to justify the suggestion that, though the high notification-rates of 1950, as compared with 1938, can largely be discounted, certain groups were perhaps still suffering a higher incidence of tuberculosis in 1950 than before the war. Since 1950, mortality has continued to decline much faster than the notification-rate.

This volume also notes that, age for age and for both sexes, mortality from all causes is higher in the north of England and in Wales than in the east or south of England. There is no sign that this difference can be attributed to simple differences in age constitution or urbanisation; it "must arise from differences in industrial or social environment (including diet) or climate or genetic influences." It seems that the northern excess of mortality "is to some extent associated with greater crowding of the population . . . and possibly the diminished sunlight and greater atmospheric pollution. . . ."

The Registrar-General has also just published the civil-tables volume [3] of his Statistical Review for 1952.

Poliomyelitis

For the first time since 1948 there have been fewer than 100 poliomyelitis notifications in England and Wales in each week up to mid-August. In the five weeks up to and including the week ended Aug. 21, the weekly totals (paralytic and non-paralytic) were 91, 95, 82, 95, and 89. In the corresponding weeks last year the figures were 266, 270, 297, 318, and 271.

The National Fund for Polio Research has issued, with the approval of the Ministry of Health, a striking leaflet which incorporates some of the advice to contacts given in the Ministry's recent memorandum.[4] The leaflet emphasises the importance of certain simple precautions when poliomyelitis is around:

"Do not share your towel, toothbrush or nail-brush with others. When your handkerchief is soiled, change it and put it in water until it can be boiled. Wash your hands thoroughly before eating or handling food. Wash your hands after using the lavatory. Keep your finger nails short and clean."

And for known contacts:

"Keep at arm's length from other people. If possible sleep in a separate bed or, better still, in a separate room. Avoid crowds and do not travel if you can help it. Keep in the fresh air as much as you can. See that your children do not play with other children. Keep them in your house and garden, or in the open fields. Avoid swimming baths, paddling pools, or other places where there are likely to be a lot of children or grown-ups. If you feel unwell, rest—and call the doctor."

Limits for Lead in Foods

The Minister of Food has approved for publication a revised report,[5] presented to the Food Standards Committee by their metallic contamination subcommittee, recommending the introduction of limits for lead in foods. An earlier report by the subcommittee was published in December, 1951.[6] Since then the subcommittee have reviewed the representations received from trade and other interests, and the revised report replaces the earlier one. The new report recommends that statutory effect should be given to the limits now proposed and that any statutory limit prescribed should be reviewed from time to time. The Food Standards Committee have adopted the report, and before taking any action on it the Minister of Food will receive any further representations which interested parties may wish to make.

The subcommittee have proposed the lowest limits which they consider can at present be readily attained under conditions of good commercial practice; they think that it should be possible, in due course, to reduce the limits proposed for a number of items, including beer, cider, wines, iced lollies, pectins, and food colourings. They confirm the appropriateness of the general limits previously recommended—i.e., 0·2 parts of lead per million (p.p.m.) for beverages ready to drink and 2 p.p.m. for other foods. For a few foods they recommend a lower limit than 2 p.p.m. On the other hand, their original inquiries, and subsequent representations, have drawn attention to items of food and drink to which these general limits could not at present be applied—principally foods liable to contamination from the container, concentrated foods, and substances in the nature of food adjuncts which are only consumed in small quantities. The foods and drinks which cannot

1. *Lancet*, 1949, i, 32.
2. The Registrar-General's Statistical Review of England and Wales for the year 1950. Text, Medical. H.M. Stationery Office. Pp. 225. 6s. 6d.
3. The Registrar-General's Statistical Review of England and Wales for the year 1952. Tables, part II, civil. H.M. Stationery Office. Pp. 184. 6s.
4. See *Lancet*, July 24, 1954, p. 187.
5. Food Standards Committee Report on Lead. H.M. Stationery Office. Pp. 11. 6d.
6. See *Lancet*, 1951, ii, 1147.

be brought within the general limits or which can be subjected to lower limits are set out in detail in the report. As for shell-fish and crustacea in which lead may occur naturally in amounts higher than 2 p.p.m., the sub-committee recommend that the sale of these foods containing lead in excess of 2 p.p.m. be permitted if it can be shown that the lead is natural to the fish.

Infestation of a Milk Bottle

The report for 1953 of the chief sanitary inspector of Leeds, Mr. James Goodfellow, mentions an instance in which a milk bottle became infested with the puparia of drosophilinæ. A housewife drew attention to a bottle of milk delivered to her home the day before; the puparia of the insect could be easily seen adhering to the inside of the bottle. It seems that the larval stage of this insect, but not the pupa, is removed by the ordinary commercial process of bottle-washing adopted by large dairies. The report points out that infestation of this kind can be prevented by rinsing the bottle as soon as it is emptied, so that the milk residue is removed. Mr. Goodfellow emphasises that dairy companies should teach their customers to rinse the bottles immediately after emptying them and before they are put outside for the milkman to collect.

A Danger from Cement

Last year the medical officer of health for Bristol, Dr. R. H. Parry, received an unusual complaint, which is discussed in his annual report for 1953. Workmen using cement on a certain site were affected by nose-bleeding and intestinal disorders, which, it was said, were caused by a gas given off when the cement was being mixed. The cement—a German product—was found to be very much finer in texture than English cement, and when it was mixed with water it gave off an acetylene-like smell. Pure acetylene is generally held to be odourless, and the smell commonly associated with it is that of an impurity, phosphine; and phosphine was, in fact, identified in the cement at Bristol. If one of the impurities in cement happens to be a phosphate, the calcining process might produce calcium phosphide, which, on contact with water, would give phosphine gas. And this could undoubtedly cause the symptoms complained of. Moreover, the unusually small cement particles would be inhaled more readily than those of English cement, and they could easily have caused trouble by lodging in the nose and throat. The offending batch of cement had been used up, but the information was sent to cement importers and others interested.

Obituary

JAMES AUBREY TORRENS
M.D. Lond., F.R.C.P.

Dr. J. A. Torrens, consulting physician to St. George's Hospital, London, died on Aug. 23 at Haslemere.

He was born in 1881, the son of Henry C. Torrens and the grandson of William McCullagh Torrens, M.P. At St. Paul's School he obtained the entrance and senior scholarships and the leaving exhibition in science, and he continued this prizewinning record by obtaining the entrance scholarship, and the anatomy, physiology, and Brodie prizes at St. George's Hospital. After qualifying in 1905, he held house-appointments at George's, subsequently becoming assistant curator of the museum and medical registrar. Later he joined the staffs of the Chelsea Hospital for Women and Paddington Green Children's Hospital. He was appointed assistant physician to St. George's shortly before the first world war, in which he served almost continuously, from 1914 till after the Armistice in 1918, in France and in Mesopotamia.

On his return to civilian life he became dean of the medical school at St. George's—an office which he held till 1926. His tenure of the post contributed largely to the renascence of the medical school, whose numbers had shrunk during the war. In 1921 he was elected F.R.C.P. He examined for the Society of Apothecaries, the Conjoint Board, and the University of Oxford.

At the outbreak of the late war he took up a whole-time post as physician in the E.M.S. at the West Middlesex Hospital, and there he spent the remainder of his professional life. In that post he was active and happy and he gained the respect and affection of his new colleagues, contributing much to the medical strength of the hospital, where his experience and counsel were highly valued.

A. F., whose acquaintance with Torrens, begun on the banks of the Tigris, quickly ripened into a warm friendship, writes: "A factual epitome of Torrens' medical life fails to do justice to his personality and to the affection and esteem in which he was held by his colleagues, pupils, and patients. He published few papers and took little part in medical societies and discussions, but his keen intelligence, active and lively mind, considerable clinical ability, and sure foundation of learning made him an excellent all-round physician and a stimulating teacher.

"His chief hobbies were racing and bridge-playing; at one time he was generally believed to own a share in a horse and he was certainly an earnest and faithful student of the racing calendar: as a bridge-player he was an acknowledged expert. Beneath a somewhat cynical manner he concealed a sensitive and friendly disposition. Always averse from publicity of any kind he could, and on rare occasions did, rise to considerable heights of eloquence in his speeches and addresses."

In 1910 Dr. Torrens married Hilda, daughter of the Rev. William Martin. She died in 1944. There was one daughter of the marriage who survives him with his second wife, Elizabeth, daughter of Mr. W. Chapman.

DONALD THOMAS FRASER
M.C., B.A., M.B. Toronto, F.R.S.(C.)

Dr. Donald Fraser, professor of hygiene and preventive medicine in the University of Toronto and associate director of the Connaught Research Laboratories, died in Santiago, Chile, on July 19 at the age of 65. Early in June he had set out on a tour of South American medical schools and schools of public health under the auspices of the Pan-American Sanitary Bureau and at the request of the World Health Organisation.

After graduating M.B. at the University of Toronto in 1915 he joined the R.A.M.C. and served in Egypt and France, where he won the Military Cross. Later, after being invalided home, he served again in China with a British Expeditionary Force when he was mentioned in despatches. On his return to Canada he joined the staff of the Connaught Laboratories and School of Hygiene of Toronto University which had lately been set up under the directorship of Dr. J. G. FitzGerald. For the next twenty years Fraser took a leading part in laboratory researches and in field studies in the campaign for immunisation against diphtheria. He was keenly interested in the methods of teaching preventive medicine to undergraduate and postgraduate students and was one of the leaders in the group that made the Toronto School of Hygiene and the Connaught Laboratories world-famous.

R. C. writes: "A quiet modest man of sterling character and great industry and determination, Don Fraser was respected and admired not only by his colleagues in Toronto but throughout North America where he was an active member of both the Canadian and American Public Health Associations and the Associations of Immunology and Epidemiology. His sage advice was often sought on the teaching and practice of preventive medicine."

H. B. M. recalls him as "one of those rare selfless persons whose gift for friendship, personal charm, and quality created affection and admiration, not only among his immediate colleagues past and present, but in a much wider circle of acquaintances, particularly in Canada and the United States. As a bacteriologist and immunologist he stood for the highest quality of attainment and he added to this an interest in the cultural and artistic life of Canada which gave him an all-round academic distinction in the best tradition. He will long be remembered."

Professor Fraser is survived by his wife, Mary Elsie, daughter of the late Dr. Joseph M. Shenstone, a distinguished Canadian surgeon, a married daughter, two sons, one of whom is medically qualified, and a foster-daughter.

Notes and News

PYROGENS

IT has long been known that fever sometimes follows the intravenous administration of drugs. Siebert [1-3] showed that these "injection fevers" are due to products of bacteria; and for these products she adopted the term "pyrogen," coined by Burdon-Sanderson. Since this pioneer work there has been much research into the nature and properties of pyrogens. Present knowledge is summarised in the proceedings of a symposium arranged by the Pharmaceutical Society and the biological methods group of the Society of Analytical Chemistry.[4]

In the first paper T. D. Whittet outlines the possible sources of pyrogens and shows how they can be eliminated from injection solutions. Clearly, pyrogen-free injections can be prepared without elaborate equipment. The *British Pharmacopœia* has since 1948 included a test for absence of pyrogens for water for injection, and the 1953 edition stipulates tests for several drugs which may be contaminated with pyrogens as a result of their method of preparation. Unlike the *United States Pharmacopœia*, the *B.P.* does not yet subject to control all of the many substances infused intravenously, and most speakers at the symposium agreed that this should be done in future editions. In addition to their hyperthermic action, pyrogens affect the leucocyte-count, causing leucopenia about half an hour after injection followed by leucocytosis some two hours later. Both these changes have been suggested as possible methods of assay, and Miss M. Dawson and Prof. J. P. Todd described results showing good correlation between the dose of pyrogen injected and the resulting leucopenia. If this is established for all pyrogens the method will be useful for detecting pyrogens in drugs which have an antipyretic action. In the last paper W. L. M. Perry described convincing evidence of the production of antiserum to pyrogens. In the discussion it was generally agreed that pyrogens are predominately polysaccharide, although apparently glucosamine units and possibly ribosenucleic acid residues may be present in some samples.

Pyretotherapy has, of course, been used for many years in the treatment of gonococcal arthritis and neurosyphilis; the hyperthermic agents used are T.A.B. vaccine or an *Escherichia coli* vaccine, which depend for their action on the pyrogens contain. In America and on the Continent pyrogens have lately been used in the pyretotherapy of several diseases, including disseminated sclerosis and malignant hypertension; and a purified pyrogen from *Pseudomonas pyocyanea* is marketed in America.

SMALL-LIST DOCTORS

THE new arrangements for the remuneration of general practitioners with small lists, recommended by the Working Party earlier this year,[5] have now been accepted by the representatives of the profession and by the Minister of Health (E.C.L. 50/54). The new scheme of "supplementary annual payments" will almost always be more advantageous than the old "hardship payments." A few doctors may be adversely affected, but they will be entitled to apply to their executive council to continue under the old scheme. Applications to enter the new scheme with retrospective effect to April 1, 1953 (or a later quarter), should be made within the next three months.

COURSES FOR MENTAL NURSES

QUALIFIED mental nurses are few and valuable. During the working life of many of them there has been a revolution in mental treatment for which they have had no formal training. The Ministry of Health is therefore urging, in a circular [6] addressed to regional hospital boards, hospital management committees, and boards of governors, that they should be offered refresher courses, arranged in their own areas. The Ministry also draws attention to the courses in nursing administration arranged by the Royal College of Nursing, and by King Edward's Hospital Fund for London, and further points out that matrons and ward sisters in the mental-hospital service are also eligible to attend the residential courses given at the King's Fund Staff Colleges for Matrons and Ward Sisters; and they should be encouraged and released to take them.

In each region, the Ministry suggests, a centre for organising short courses for all grades of qualified mental staff should be set up in a hospital where the standards of nursing care and management are high. Courses should last about a fortnight, and those taking them should be given travelling and subsistence allowances, and should be housed in or near the hospital. They should gain experience of modern methods of treatment in various types of ward, should join in talks and discussions, and should pay visits to other hospitals to study special points in mental nursing. Classes of about 12 are suggested, and the mental nursing officers of the Ministry will advise, if wished, on the content and organisation of the courses. If any hospital finds it impossible to release members of the trained staff for two weeks at a stretch, courses requiring attendance for one or two days a week over a period of time may be arranged; but the Ministry points out that this arrangement sacrifices many of the advantages of a residential course, and can only be regarded as a second best.

MEDICAL BIBLIOGRAPHY

THE first large-scale history of medical bibliography, published in the U.S.A.,[1] is the fruit of four years' research. Estelle Brodman, the author, began by finding out what bibliographies existed, examining personally all that were available, and assessing the historical significance of each. Her general conclusion is that there is still no technique for covering all medical literature accurately and promptly, and that for the present we must be content with the feasible compromises.

It was the invention of printing that gave rise to modern medical bibliography, and the first chapter, on the sixteenth century, contains valuable appraisals of such pioneers as Champier, Brunfels, and Gesner. The second chapter is on the seventeenth century, in which the main advances were made by Linden, Lipenius, and Beughem; a new problem was the recording of articles in periodicals. The eighteenth century, the subject of the third chapter, was the golden age of individual bibliographies, and is dominated by Haller, of whom an excellent account is given. The fourth chapter is on the growth of coöperative bibliography in the nineteenth century; the outstanding figure is John Shaw Billings, whose ideas continue to unfold in our own day. The closing chapter is a comprehensive discussion of contemporary problems in medical bibliography. From this discussion, as indeed progressively from the earlier chapters, medical bibliography emerges as a most difficult art, nowadays aided by mathematics and electronics, but requiring, as always, high intellect for its direction.

The volume will certainly take its place as one of the standard textbooks for medical librarians; its abundant references will make it indispensable to students of medical bibliography; and it will interest and enlighten all who write or read medical literature.

ALLOCATIONS TO REGIONAL HOSPITAL BOARDS

THE sum available for distribution among the wards for capital expenditure during 1955–56 is the same as for 1954–55 (HM[54]74), and the allocation to each board is also to be unchanged. The level of capital investment for 1956–57 cannot yet be foreseen, but boards are asked to assume that no more money will be available than in the preceding year. The Minister of Health once more urges boards to give priority to schemes which will provide more accommodation for mentally ill and mentally defective patients.

BRITISH STANDARDS YEARBOOK

THE 1954 edition of *British Standards Yearbook* lists 2500 British Standards current at March 31, and briefly describes the subject matter of each. Copies (price 12*s.* 6*d.*) may be had from the British Standards Institution, British Standards House, 2, Park Street, London, W.1.

1. Seibert, F. B. *Amer. J. Physiol.* 1923, **67**, 90.
2. Seibert, F. B., Mendel, L. B. *Ibid*, 1923, **67**, 105.
3. Seibert, F. B., Mendel, L. B. *Ibid.* 1925 **71**, 652.
4. Assay and Detection of Pyrogens. London: Pharmaceutical Press. 1954. Pp. 43. 3*s.* 6*d.*
5. See *Lancet*, 1954, i, 975; *Brit. med. J.* 1954, i, suppl. 206.
6. H.M.(54)72.

1. The Development of Medical Bibliography. By ESTELLE BRODMAN, assistant librarian for reference services, Armed Forces Medical Library, Washington, D.C. Baltimore: Medical Library Association. 1954. Pp. 226. $5.

Society of Apothecaries of London

The following diplomas have been granted:

M.M.S.A.—J. Wessels.

L.M.S.S.A.—W. R. Peniston, N. W. Fogg, G. W. Carp, R. D. H. Kelly, C. G. Young, H. A. Williams, C. D. Chilvers, N. S. Halaby, R. G. Tarrant, B. W. Subhyah, B. C. Roughton, K. P. Walker, R. V. F. *Williams, L. R. Jenkins, M. M. Adams, S. K. Young, T. H.* Harries, B. R. Morgan, R. J. W. Adamson, P. F. Stebbing, M. H. Khatan, R. D. Lowe, A. Danillowicz, J. A. Maling, A. M. Lindsay, M. N. *Khurshid*, F. C. V. *Brightman*, J. Grey, A. J. Lacey, R. Young, H. Backer, L. W. Reeves, D. V. Burke, S. Jones, R. M. Stewart, N. W. Sargent, G. Codd, E. S. Price, S. M. Jamaldeen, W. P. Neville, E. R. Frohlick, B. S. N. Hsu, P. Stanesby, D. W. Griffith, M. R. G. Houri, A. R. Matthews, G. L. Goodwin, D. K. Brooks, Chan Ban, S. R. Hunt, A. M. Freeman.

D.I.H.—S. M. Bieber, R. B. Body, J. Cameron, R. L. Luffingham, *W. M. McCutcheon, P. C. Murray*, F. W. Newby-Good, B. L. Shapiro, K. M. Williams, J. D. Stewart.

St. Thomas's Hospital

The old students' dinner of this hospital will take place at the Royal College of Surgeons, Lincoln's Inn Fields, W.C.2., on Thursday, Oct. 7, at 7.30 P.M. Sir Max Page will be in the chair. Tickets (£1 10s.) may be had from the hon. secretaries, St. Thomas's Hospital Medical School, London, S.E.1.

Institute of Mental Health in India

The first Indian institute of mental health was opened in Bangalore, Southern India, on Aug. 7 by Rajakumari Amrit Kaur, the Indian minister of health. It is planned as a post-graduate teaching and research centre for psychiatry, affiliated to Mysore University, and its first director is Dr. M. V. Govindaswamy. The institute was initiated by W.H.O., which two years ago sent out Dr. W. Mayer-Gross, of Dumfries, for the planning of the project.

Conference on Occupational Chest Diseases

A conference on silicosis and occupational chest diseases, sponsored by the McIntyre Research Foundation of Toronto, Canada, and the Saranac Laboratory of Saranac Lake, New York, is to be held from Feb. 7 to 9, at Saranac Lake, under the chairmanship of Prof. Anthony J. Lanza. Further details may be had from the secretary, Saranac Laboratory, Saranac Lake, New York.

Fédération Internationale Pharmaceutique

The next assembly of the federation is to be held in London from Sept. 19 to 23, 1955. It is expected that some 1200 delegates from 40 different countries will attend. The secretary of the organising committee is Mr. D. F. Lewis, F.P.S., 17, Bloomsbury Square, W.C.1.

Chief Medical Officer for Northern Ireland

Dr. F. F. Main has been appointed chief medical officer in the Northern Ireland ministry of health and local government, in succession to Dr. James Boyd who is retiring.

Dr. Main, who is a native of Edinburgh, was educated at Daniel Stewart's College, Edinburgh, and Edinburgh University, from which he graduated M.B. in 1927. He held house-appointments at the Edinburgh Royal Infirmary, where he also served as assistant clinical pathologist. In 1931 he took the D.P.H., and soon afterwards joined the public-health service of Kilmarnock. Later he was appointed deputy medical officer of health and school medical officer for the burgh, and he held this post until 1937 when he became medical officer of health for Perth. During the late war he organised and administered the civil-defence and casualty services in Perth. Since 1948 he has been senior administrative medical officer for the Scottish Eastern Regional Hospital Board.

Awards in Radiological Research

On behalf of the James Picker Foundation, the National Academy of Sciences-National Research Council are again offering grants and fellowships for radiological research. Awards are not restricted to citizens of the United States.

Grants-in-aid are designed to encourage research offering promise of improvement in radiological methods of diagnosis or treatment of disease. Applications for 1955–56 must be submitted by Nov. 30, 1954.

Grants for scholars are designed to bridge the gap between the end of fellowship training and the period when the young scientist has shown his competence as an independent investigator. A grant of $6000 per year will be made directly to the scholar's institution as a contribution toward his support, or his research, or both. Applications for 1955–56 should be submitted by the institution before Nov. 30, 1954.

Fellowships are designed to offer research experience to promising postgraduates. Candidates should usually be no more than thirty-five years of age. Applications for 1955–56 must be postmarked on or before Dec. 10, 1954.

Further details may be had from the division of medical sciences of the council, 2101, Constitution Avenue, N.W., Washington 25, D.C.

Homosexuality Inquiry

The following have been appointed to the committee which, under the chairmanship of Mr. J. F. Wolfenden, vice-chancellor of Reading University, is to inquire into the laws relating to homosexual offences and prostitution:

Mr. James Adair, formerly procurator-fiscal at Glasgow; Mrs. Mary Cohen, chairman of the Scottish Association of Girls' Clubs; Dr. Desmond Curran, senior psychiatrist, St. George's Hospital, and civilian consultant in psychological medicine to the Royal Navy; the Rev. V. A. Demant, regius professor of moral and pastoral theology at Oxford; Mr. Kenneth Diplock, Q.C., recorder of Oxford and a member of the Lord Chancellor's Law Reform Committee, 1952; Sir Hugh Linstead, M.P. for Putney and secretary of the Pharmaceutical Society; Lord Lothian; Mrs. Kathleen Lovibond, chairman of Uxbridge juvenile courts; Mr. Victor Mishcon, chairman of the London County Council; Mr. Goronwy Rees, principal of the University College of Wales at *Aberystwyth*; Lady Stopford, M.B., a magistrate; the Rev. R. F. V. Scott, minister of St. Columba's (Church of Scotland), Pont Street, S.W.1; Mr. W. T. Wells, M.P. for Walsall and a member of the Lord Chancellor's Committee on the Practice and Procedure of the Supreme Court, 1947–53, and of the Magistrates' Courts Rules Committee; and Dr. Joseph Whitby, M.R.C.P., D.P.M., a general practitioner in north London and formerly assistant physician to the Maudsley Hospital.

The secretary of the committee is Mr. W. C. Roberts, of the Home Office. Mr. E. J. Freeman, of the Scottish Home Department, has been appointed assistant secretary.

Award for Lord Nuffield

The International Society for the Welfare of Cripples and the Albert and Mary Lasker Foundation announce that the Albert Lasker award will be presented to Lord Nuffield on Sept. 15 at the world congress of the society at The Hague. The award is given for "outstanding achievement in the development of services for the physically disabled." Lord Nuffield is president of the Central Council for the Care of the Cripples in Britain and of the British Rheumatic Association and has done much to provide care and treatment for cripples in Britain, Australia, New Zealand, and South Africa.

A Rockefeller Grant

The awards announced in the Rockefeller Foundation's second quarterly report for 1954 include a grant of $80,000 to Prof. H. A. Krebs, F.R.S., and his colleagues at Sheffield University for continued research in cell metabolism. The report states that the research of Dr. Krebs and his colleagues is now centring on the chemical mechanisms by which the living cell utilises foodstuffs and the energy they provide. The programme is proceeding along four main avenues: biological energy transformations; synthetic processes; properties of enzymes; and elaboration of methods in biochemistry.

Appointments

COWIE, JOHN, M.B. Aberd., D.P.M.: part-time senior hospital M.O., department of psychiatry, The London Hospital.

EDMUNDS, P. N., M.B., B.SC. Edin.: bacteriologist (S.H.M.O.), Astley Ainslie Hospital, Edinburgh.

EDWARDS, C. H., M.R.C.P.: part-time consultant, department of nervous diseases, St. Mary's Hospital, London.

FALCONER, T. C., M.B. St. And., D.P.H.: asst. M.O., West Lothian.

HOWORTH, IRENE E., M.B., B.SC. Manc., D.OBST., D.P.H.: chief asst. county M.O.H., Lancs.

LACK, C. C., M.R.C.S., D.P.M.: consultant in child psychiatry, The London Hospital.

MEANOCK, R. L., M.D. Lond., M.R.C.P.: consultant in physical medicine, Reading and district H.M.C.S.

MILLER, S. J. H., M.D. Aberd., F.R.C.S., D.O.M.S.: part-time consultant surgeon, Moorfields, Westminster, and Central Eye Hospital, to attend Westminster branch.

MORLEY-DAVIES, R. B., M.B., B.SC. Wales, D.P.H.: M.O.H. for Rhondda and divisional M.O., Glamorgan.

MUNRO, D. E., M.B. Glasg., D.P.M.: whole-time psychiatrist as deputy physician-superintendent (S.H.M.O. grade), Dingleton Mental Hospital, Melrose.

RAE, A. S. L., M.D. Edin., D.P.H., D.P.M.: whole-time deputy physician-superintendent, Dundee District Mental Hospital.

ROBERTSON, J. DOUGLAS, M.D., D.SC. St. And., F.R.C.P., F.R.I.C., D.P.H.: consultant chemical pathologist, West London Hospital.

SWAN, H. T., M.B. Edin., M.R.C.P., D.C.H.: whole-time asst. hæmatologist (S.H.M.O.), United Sheffield Hospitals.

TOVEY, L. A. D., M.B. Brist.: registrar, South West Regional Blood Transfusion Centre, Southmead, Bristol.

WEITZEN, PAUL, M.B. Polish School of Medicine, Edinburgh: whole-time asst. anæsthetist (S.H.M.O. grade), West Fife.

WOOLGROVE, C. G., M.B. Birm., D.P.H.: asst. county M.O.H., Derbyshire, and M.O.H., Shardlow.

Appointed Factory Doctor:

HOUSE, A. V., M.R.C.S.: Bicester, Oxford.

WYLIE, G. L., M.B. Glasg.: Duns, Berwick.

Hertfordshire County Council:

GILLESPIE, J. C., M.B. Glasg., D.C.H., D.P.H.: asst. M.O.

SHORE, ELIZABETH C., M.R.C.S., D.OBST.: asst. M.O.

WALKER, J., M.B., D.C.H.: asst. M.O.

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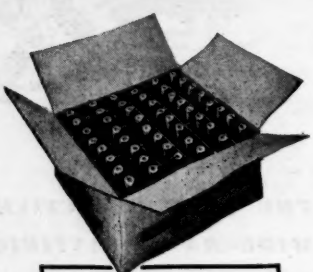

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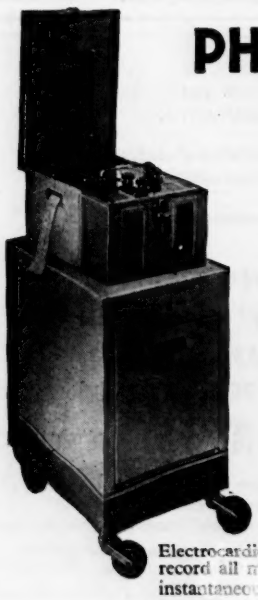

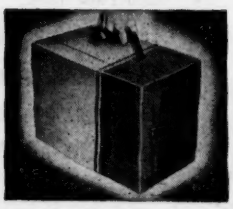

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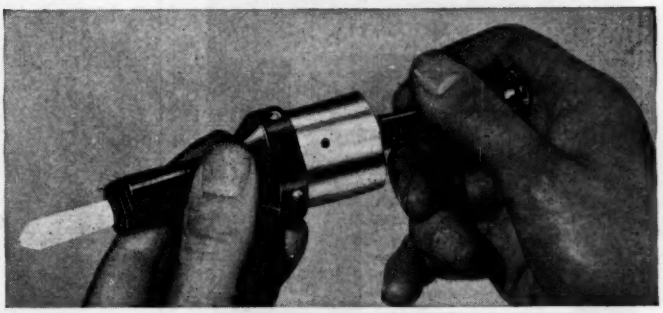

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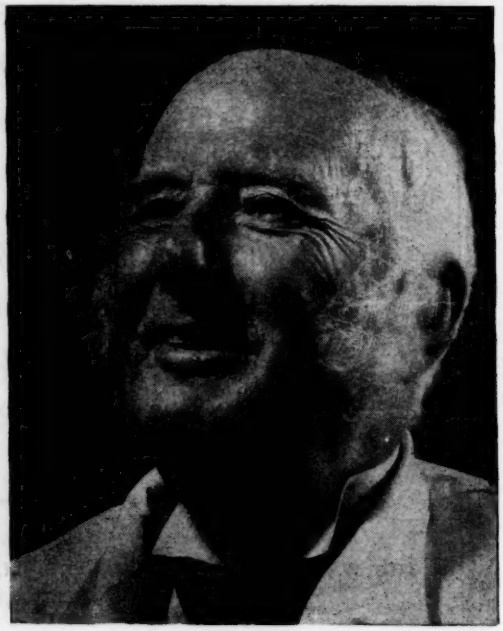

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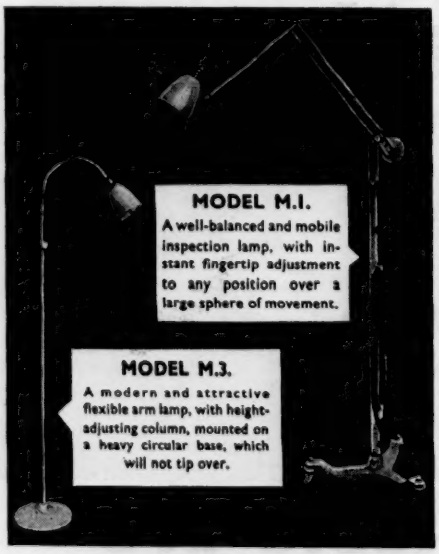
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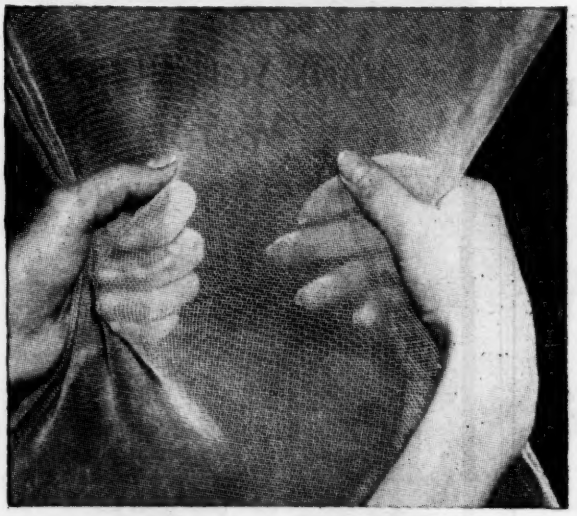

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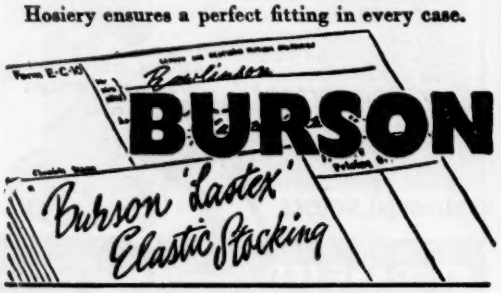

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COURSE ON POLIOMYELITIS
11TH–15TH OCTOBER

MONDAY, 11TH OCTOBER, TOWN SECTION

The Virus and the Environment	Dr. F. O. MACCALLUM
Open discussion on above	Dr. F. O. MACCALLUM
The Pathological Anatomy of Poliomyelitis and its bearing on clinical features, including prognosis and recovery	Dr. H. A. SISSONS and Mr. W. J. W. SHARRARD

TUESDAY, 12TH OCTOBER, COUNTRY SECTION

Treatment in convalescent phase: muscle charts: electrical examination	Mr. D. M. BROOKS and Miss L. M. PRIOR
Respiratory and bulbar paralysis	Dr. A. B. KINNIER-WILSON and Dr. F. H. STEVENSON

WEDNESDAY, 13TH OCTOBER, COUNTRY SECTION

Reconstructive surgery	Mr. J. A. CHOLMELEY
Afternoon—GARSTON MANOR REHABILITATION CENTRE, NEAR WATFORD, HERTS.	
Rehabilitation	Group Captain C. J. S. O'MALLEY

THURSDAY, 14TH OCTOBER, TOWN SECTION

Vascular phenomena	Mr. G. L. W. BONNEY
Some neurological problems of diagnosis	Dr. P. H. SANDIFER

Open for informal discussion on any aspect of poliomyelitis

FRIDAY, 15TH OCTOBER, COUNTRY SECTION

Resettlement	Mr. D. M. BROOKS
Appliances: prescription	Mr. H. J. SEDDON
Appliances: construction	Mr. W. TUCK

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Cheshire Joint Sanatorium, Market Drayton, Shropshire: 27TH, 28TH, and 29TH OCTOBER, 1954. (4 places.)
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LOCKE RESEARCH FELLOWSHIP

Applications are invited by the Council of the Royal Society for the Locke Research Fellowship, tenable at any place approved by the Council of the Royal Society, for research in the general field of experimental physiology and pharmacology. Candidates should supply the usual personal details and give the names of 2 referees. Testimonials will not be considered. Applicants and referees at a distance may write direct to the address given below, without first obtaining forms. The subject of the proposed research and the place at which it would be carried out, together with the name of the Head of the Department, should be given.

The appointment will be for 2 years in the first instance, from 1st January, 1955, and may be renewed annually for such periods as Council may determine. The successful applicant may only undertake any other work concurrently with the Fellowship upon obtaining the written consent of the President and Council of the Royal Society. The stipend will be £1250 p.a., with superannuation benefits to which the successful candidate will be required to contribute 5% of annual stipend and to which the Society will make a contribution equal to 10% of the stipend.

Application should be made on forms to be obtained from the Assistant Secretary, the Royal Society, Burlington House, London, W.1, and should be received as early as possible, in any case not later than 1st October, 1954.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There is a vacancy for a RESEARCH FELLOW to work on hydrocephalus and spina bifida in the Department of Morbid Anatomy. The post is tenable in the first instance for 1 year and the salary will not be less than £1000 p.a., depending on experience and qualifications. Further particulars of the post may be obtained on application to Dr. M. Bodian at the Hospital.

Forms of application, which should be returned by 1st October, 1954, are obtainable from the undersigned. (Candidates should indicate proposed line of research).

H. F. RUTHERFORD, House Governor and Secretary.

INSTITUTE OF BASIC MEDICAL SCIENCES

ROYAL COLLEGE OF SURGEONS OF ENGLAND
BRITISH POSTGRADUATE MEDICAL FEDERATION
(UNIVERSITY OF LONDON)

Applications are invited from candidates with medical qualifications for the full-time post of LECTURER IN PHYSIOLOGY. The successful candidate will be expected to take part in the teaching activities of the Department of Physiology. Facilities for research are available both in the laboratories of the Department and the Buckston Browne Research Farm of the Royal College of Surgeons. Salary will be within the University scale of £800–£100–£1100 p.a. together with membership of the F.S.S.U. The commencing salary will be determined by the age, qualifications, and experience of the successful candidate. The choice will not be limited to those who make formal application and the right is reserved to fill the post by invitation.

Applications (3 copies), together with the names of 2 referees, should be sent not later than 14th October, 1954, to Prof. David Slome, M.A., PH.D., M.B., CH.B., Department of Physiology, Royal College of Surgeons, Lincoln's Inn-fields, W.C.2, from whom further particulars may be obtained.

W. F. DAVIS, Secretary.

THE HEBERDEN SOCIETY

On FRIDAY, 24TH SEPTEMBER, 1954, at 5 P.M., Dr. ROBERT M. STECHER, of Cleveland, Ohio, U.S.A., will give the HEBERDEN ORATION FOR 1954 at the Postgraduate Medical School of London, entitled "Heberden's Nodes."

Members of the medical profession are cordially invited to attend.

LEEDS REGIONAL HOSPITAL BOARD, in association with the University of Leeds, invites applications for the post of RESEARCH REGISTRAR IN RHEUMATISM to assist the Professor of Clinical Medicine with research projects at the Royal Bath Hospital, Harrogate, which is the centre for the Regional Rheumatism Scheme. Accommodation available for a single person, if required.

Applications, stating age, qualifications and details of present and previous appointments with dates, together with the names and addresses of 3 referees, should be forwarded to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, not later than Thursday, 16th September, 1954.

STOKE MANDEVILLE HOSPITAL, Aylesbury, Buckinghamshire. OXFORD REGIONAL RHEUMATISM RESEARCH CENTRE. Applications are invited for the appointment of RESEARCH ASSOCIATE to undertake studies of certain aspects of tissue immunology and the rôle of antigen-antibody reactions in disease. Consideration will be given to applicants interested exclusively in laboratory research, but opportunities for clinical work could be provided for a suitable candidate, who would receive remuneration (provided from a grant made by the Nuffield Foundation) in the Senior Registrar grade.

Applications should be made to the Director of the Centre, from whom further details can be obtained.

THE UNIVERSITY OF LIVERPOOL. Applications are invited for the 2 part-time posts of LECTURER IN PSYCHIATRY, and LECTURER IN CHILD PSYCHIATRY, at a remuneration of £200 p.a. each. The duties of the successful applicant will be in connection with the postgraduate course in psychiatry which will commence on 1st January, 1955.

Applications, stating age, qualifications and experience, together with the names of 2 referees, should be received not later than 5th October, 1954, by the undersigned, from whom further particulars may be obtained.

STANLEY DUMBRELL, Registrar.

THE UNIVERSITY OF MANCHESTER. Applications are invited for the post of LECTURER IN DENTAL SURGERY in the Turner Dental School. Candidates should have dental qualifications registrable in this country, and preferably some experience in dental bacteriology and pathology in which excellent opportunities for research exist. Salary on a scale rising to £1800 p.a.; initial salary according to qualifications and experience. Membership of the F.S.S.U. and children's allowance scheme in force.

Applications should be sent not later than 2nd October, 1954, to the Registrar, the University, Manchester, 13, from whom further particulars and forms of application may be obtained.

THE UNIVERSITY OF SHEFFIELD. Applications are invited for a post of LECTURER or SENIOR LECTURER IN SURGERY to begin duties as soon as possible. Salary scales: Lecturer, £700–£100–£1500; Senior Lecturer, £1500–£100–£2000; with F.S.S.U. provision and family allowance. Initial salary on either scale according to qualifications and experience.

Further particulars should be obtained from the Registrar, to whom applications (4 copies) should be sent by 2nd October, 1954.

THE UNIVERSITY OF SHEFFIELD. Applications are invited for a post of SENIOR LECTURER or LECTURER IN PATHOLOGY to begin duties as soon as possible. Salary scales: Senior Lecturer, £1500–£100–£2000; Lecturer, £700–£100–£1500, with F.S.S.U. provision and family allowance. Initial salary for a Lecturer according to qualifications and experience.

Further particulars should be obtained from the Registrar to whom applications (4 copies) should be sent by 2nd October, 1954.

Hospital Services: Senior Appointments

ST. PETER'S, ST. PAUL'S AND ST. PHILIP'S HOSPITALS, Henrietta-street, W.C.2. Required for 1st January, 1955, CLINICAL PATHOLOGIST of Consultant grade. Full-time. Main interest to be morbid histology. To have general charge of the laboratories.

Applications (9 copies), giving age, experience, grade, and names of 3 referees, to House Governor. Closing date 2nd October, 1954.

HOSPITAL OF ST. JOHN AND ST. ELIZABETH, 60, Grove End-road, London, N.W.8. Applications are invited for the post of HONORARY CONSULTING PHYSICIAN to the new Children's Department. Candidates must be a Member or Fellow of one of the Royal Colleges of Physicians.

Applications (30 copies), should be sent to the undersigned on or before Monday, 18th October, 1954. Testimonials are not required but the names of 3 persons willing to act as referees should be furnished. Sister MARY CLARE, Secretary.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.

1. CONSULTANT OBSTETRICIAN AND GYNÆCOLOGIST (part-time), City of London Maternity Hospital (71 Beds) and Clinic for 1 half-day a week.

Applications by 1st October, 1954.

2. CONSULTANT GENERAL PHYSICIAN (part-time) at Brentford Hospital, Middlesex (33 Beds), and Teddington, Hampton Wick, and District Hospital, Middlesex (51 Beds), for 1 half-day a fortnight at each.

Applications by 8th October, 1954.

Hospitals and Clinic may be visited by direct appointment.

3. CONSULTANT in Physical Medicine (whole-time or maximum sessions). Duties at Garston Manor Rehabilitation Centre, near Watford, Herts (55 Beds), for 4 half-days a week, and Mid Herts and Luton and Hitchin groups of hospitals for the remainder. Successful candidate required to live within easy reach of Garston Manor and may need to be resident for 2 nights a week during the next year or so. A cottage on the estate may be rented if desired.

Applications by 13th October, 1954.

Centre and hospitals may be visited by appointment with Group Secretaries at 9, Rickmansworth-road, Watford; Bleak House, Catherine-street, St. Albans; St. Mary's Hospital, Dunstable-road, Luton, respectively.

Application forms obtainable from and returnable to Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, London W.1.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

Full-time ASSISTANT CHEST PHYSICIAN (Senior Hospital Medical Officer grade) at Tottenham Chest Clinic, St. Ann's General Hospital, N.15, and for 140 tuberculosis beds. The Clinic is closely associated with the Thoracic Surgery Unit at North Middlesex Hospital, N.18. Candidates should have good general medical experience and special experience in tuberculosis and diseases of the chest.

Part-time CONSULTANT E.N.T. SURGEON, Rush Green Hospital, Romford, Essex (4 sessions a week).

Part-time CONSULTANT E.N.T. SURGEON, Waltham Abbey War Memorial Hospital, Essex (1 session a week).

Applications (6 copies), stating post concerned and names of 3 referees, should reach the Secretary, 11A, Portland-place, London, W.1, by Saturday, 18th September, 1954.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Part-time CONSULTANT in E.N.T. Surgery (4 notional half-days a week) to the Camberwell group of hospitals. The duties will include outpatient clinics, operating sessions and charge of beds at St. Giles' Hospital, St. Giles'-road, Camberwell, S.E.5, and sessions will be on the following days: Monday, P.M.; Wednesday, P.M.; Friday, A.M. and P.M. Candidates must have had wide experience in E.N.T. surgery and be Fellows of a Royal College of Surgeons. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales). Candidates may visit the hospitals concerned.

Apply, stating nationality, age, sex, qualifications and experience, including details of present appointment and war service, together with the names and addresses of 3 referees, to the Secretary, Advisory Appointments Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 18th September, 1954.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Part-time CONSULTANT OPHTHALMOLOGIST (1 half-day per week) for the Fulham and Kensington group of hospitals. Duties mainly at Fulham Hospital, W.6, session Monday afternoons.

Applications (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 2nd October, 1954. Applicants may visit hospitals by local arrangement.

MANCHESTER REGIONAL HOSPITAL BOARD.

(a) Whole-time NON-RESIDENT ASSISTANT ANÆSTHETIST (Senior Hospital Medical Officer) to the Lancaster and Kendal Hospitals (Royal Lancaster Infirmary, Queen Victoria Hospital, Morecambe and Westmorland County Hospital, Kendal) and at Lancaster Moor Hospital. Qualification in anæsthetics desirable. Successful candidate will work under general guidance of consultants and will be required to live in or very near Lancaster. 13th September, 1954.

(b) Whole-time CONSULTANT PATHOLOGIST to Wythenshawe (general, 350 Beds), Baguley (tuberculosis and thoracic surgery centre, 400 Beds), and Duchess of York (children, 100 Beds) Hospitals, with occasional duties at Withington Hospital, all in the South Manchester Hospital Centre. Experience of all branches of hospital pathology desirable. Successful candidate to live in area. 20th September, 1954.

(c) Whole-time CONSULTANT RADIOLOGIST in charge of diagnostic radiology at Wythenshawe (general, 350 Beds) and Baguley (tuberculosis and thoracic surgery centre, 400 Beds) Hospitals and at Manchester Chest Clinic, all in the South Manchester Hospital Centre. Wide experience and higher qualifications essential. Appointee to live in area. 22nd September, 1954.

Application forms from the Senior Administrative Medical Officer to the Board, Cheetwood-road, Manchester, 8, to be returned by dates stated.

RE-ADVERTISEMENT

LEEDS REGIONAL HOSPITAL BOARD. Whole-time ASSISTANT CHEST PHYSICIAN AND DEPUTY MEDICAL SUPERINTENDENT (Senior Hospital Medical Officer scale) at The Hospital, Grassington, Skipton (208 Beds). Residential accommodation available for a single person.

Applications (12 copies), stating age, qualifications, and details of appointments held showing dates, with names and addresses of 3 referees, to the Secretary, Park-parade, Harrogate, not later than 18th September, 1954.

LEEDS REGIONAL HOSPITAL BOARD. Locum Tenens CONSULTANT in Anæsthetics required for the Thoracic Unit, Castle Hill Hospital, near Hull, for a period of approximately 6 months.

Applications, stating age, qualifications and details of previous appointments, together with the names and addresses of 3 referees, should be forwarded to the Secretary to the Board, Park-parade, Harrogate.

OXFORD REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of DEPUTY SENIOR ADMINISTRATIVE MEDICAL OFFICER at a salary of £1550–£100–£2050. The successful applicant will be required to deputise for and to work under the general direction and supervision of the Board's Senior Administrative Medical Officer and to take up his duties on 1st April, 1955. Applicants should have considerable experience of medical administration in the health and hospital services. The post is subject to the National Health Service superannuation regulations, and may be terminated by 3 months notice on either side.

Applications, together with names of 3 referees, should reach the Secretary, the Oxford Regional Hospital Board, 43, Banbury-road, Oxford, before 1st October, 1954.

OXFORD. UNITED OXFORD HOSPITALS. Oxford REGIONAL HOSPITAL BOARD. Applications are invited for a post of CONSULTANT ORTHOPÆDIC SURGEON to the Wingfield Morris Orthopædic Hospital and the Accident Service of the United Oxford Hospitals. The post will include duties in the Wingfield Hospital, its associated clinics, and the Radcliffe Infirmary. It will be part-time for 8 half-days per week. Candidates must hold the Fellowship of a Royal College of Surgeons or equivalent higher qualification. Further information may be obtained from the Director of Orthopædic Services, Wingfield Morris Orthopædic Hospital.

Applications (15 copies), stating age, qualifications, experience, and the names of 3 referees, to the Secretary, Oxford Regional Hospital Board, 43, Banbury-road, Oxford, by 1st October, 1954.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for a part-time appointment (8 sessions) as CONSULTANT OPHTHALMIC SURGEON for duty at Bangour Hospital, Broxburn, West Lothian. This Hospital is situated some 16 miles west of Edinburgh and the Ophthalmic Unit is in process of extension to accommodate approximately 32 beds. The person appointed will be expected to take part in the development of outpatient facilities for the adjacent area as well as for the care of these beds. A proportion of the beds will be utilised for patients coming from the Royal Infirmary, Edinburgh, and, in so far as those patients are concerned, the consultant appointed will require to work in close liaison with the Ophthalmic Surgeons to the Royal Infirmary. The appointment is subject to the terms and conditions of the National Health Service.

Applications, giving particulars of age, qualifications and previous experience, together with the names of 3 referees, should be submitted to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 2nd October, 1954.

SCOTLAND. EASTERN REGIONAL HOSPITAL BOARD. Applications are invited by the Board for the appointment of SENIOR ADMINISTRATIVE MEDICAL OFFICER. The salary scale is £1850–£125–£2475 p.a. and the post is superannuable.

Further particulars and a form of application may be had from the Secretary of the Board, 430, Blackness-road, Dundee, with whom applications, giving names and addresses of 3 referees, must be lodged not later than 25th September, 1954. Canvassing, whether direct or indirect, will disqualify.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as CONSULTANT in Therapeutic Radiology to the Medway and Gravesend group of hospitals for duty at the Radiotherapy Centre at St. William's Hospital, Rochester. Candidates must have had wide experience in the specialty and hold an appropriate diploma. Choice of whole-time service or the maximum number of part-time sessions will be offered. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales). Candidates may visit the hospitals concerned.

Apply, stating nationality, age, sex, qualifications and experience, including details of present appointment and of war service, together with the names and addresses of 3 referees, to the Secretary, Advisory Appointments Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 18th September, 1954.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time ASSISTANT CHEST PHYSICIAN for Wathwood Hospital, Wath-on-Dearne, near Rotherham (104 Beds), and Allied Chest Clinics. Knowledge of pre- and post-operative care essential as primary duties will be with the Thoracic Unit. The successful candidate will work under the direction of Consultants. Candidates should have good general medical background and special experience in the treatment of chest diseases and tuberculosis. Salary scale £1500–£50–£1950.

Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, 10. Forms to be returned by 25th September, 1954.

SHEFFIELD REGIONAL HOSPITAL BOARD. Maximum Part-time CONSULTANT SURGEON required, with duties mainly at the Nottingham General and Newark Hospitals. The successful candidate will be required to reside within 10 miles of Newark.

Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, 10. Forms to be returned by 25th September, 1954.

SHEFFIELD REGIONAL HOSPITAL BOARD. Maximum Part-time CONSULTANT ANÆSTHETIST required for the Rotherham and Mexborough Hospital Management Committee Group (Doncaster Gate Hospital (161 Beds), Moorgate General Hospital (355 Beds), Rotherham, and Montagu Hospital (168 Beds), Mexborough).

Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 2nd October, 1954.

AMENDED ADVERTISEMENT

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS AND SHEFFIELD REGIONAL HOSPITAL BOARD. Applications are invited for the post of CONSULTANT RADIOLOGIST. This joint appointment may be held on a whole-time or maximum part-time basis but in either case the majority of the sessions will be held in The United Sheffield Hospitals and the remainder in the Rotherham Group of hospitals. Wide experience in the specialty is necessary and higher qualifications desirable.

Applications (16 copies), stating age, qualifications and experience, together with the names of 3 referees, should be sent to the Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield, 1 (from whom further particulars may be obtained), not later than 30th September, 1954.

WELSH REGIONAL HOSPITAL BOARD. Required immediately, West Wales General Hospital, Carmarthen, whole-time Locum Tenens CONSULTANT OBSTETRICIAN AND GYNÆCOLOGIST.

Applications, naming 2 referees, to Senior Assistant Medical Officer, Temple of Peace, Cathays Park, Cardiff.

KENYA COLONY. NAKURU WAR MEMORIAL HOSPITAL, NAKURU. The above Hospital requires the services of a fully qualified RADIOLOGIST immediately, to be engaged on 1 of the 2 following alternative bases. The Hospital is of modern construction, has 72 Beds, is fully equipped with first-class X-ray apparatus, and is served by 25 general practitioners, there being no other hospital facilities within a radius of 100 miles. The climate of Nakuru is healthy, and there are ample facilities for education, sport, &c., being situated in the centre of the European settled area.

The alternative methods of engagement are :—

1. To enable a radiologist to establish a practice at the Hospital by making available the X-ray room and apparatus at an agreed rental. The Board of Management would consider the payment of a guaranteed income over a period of 3 years, on a reducing basis, during the establishment of the practice.

2. On a basis of employment by the Hospital on contract in accordance with the normal conditions appertaining to the appointment of a fully qualified radiologist to a post of this type.

Preference will be given to applicants under the age of 35 years who are desirous of establishing themselves in the Colony, where there is ample scope for a capable man to build up a sound reputation and full facilities will be granted to attain this end.

For further particulars application should be made to the Secretaries, Nakuru War Memorial Hospital, P.O. Box 35, Nakuru, Kenya Colony.

MELBOURNE, AUSTRALIA. ST. VINCENT'S HOSPITAL. Applications are invited for the position of DIRECTOR OF ANÆSTHESIA. St. Vincent's Hospital is an Undergraduate and Postgraduate Teaching Hospital of the University of Melbourne. A salary £A3000 will be paid with a limited right of private practice. The appointment is permanent subject to a completion of an interval of 2 years probationary period. Details of appointment may be obtained from the undersigned or the Dean of the Faculty of Anæsthetists, London.

Applications close on 8th October, 1954.

E. W. R. GRACE, Secretary and Chief Executive Officer.

Hospital Services : Junior Appointments

ALBERT DOCK ORTHOPÆDIC AND FRACTURE HOSPITAL, Alnwick-road, E.16. SEAMEN'S HOSPITALS GROUP. Required 16th September SENIOR HOUSE SURGEON. Post recognised by Royal College of Surgeons.

Applications, stating age, nationality, qualifications, and experience with names of 3 recent referees, should be sent on or before 9th September to Group Secretary, Dreadnought Hospital, Greenwich, S.E.10.

ALBERT DOCK ORTHOPÆDIC AND FRACTURE HOSPITAL, Alnwick-road, E.16. SEAMEN'S HOSPITALS GROUP. Required 28th September SENIOR HOUSE OFFICER for receiving-room duties. Post which is recognised by the Royal College of Surgeons provides excellent experience in a wide variety of traumatic conditions received from the adjacent dockland and from shipping in the Port of London.

Applications, stating age, nationality, qualifications, and experience, with 2 recent testimonials, should be sent on or before 18th September to Group Secretary, Dreadnought Hospital, Greenwich, S.E.10.

BETHNAL GREEN HOSPITAL, Cambridge Heath-road, London, E.2. (General—310 Beds.) HOUSE SURGEON (gynæcology and obstetrics). Post recognised for pre-registration purposes.

Applications, stating age, experience, qualifications and copies of 2 testimonials, to the Hospital Secretary by 14th September, 1954.

ACTON HOSPITAL, Gunnersbury-lane, W.3. Senior HOUSE OFFICER (resident) required for casualty duties. Post vacant 24th September, 1954.

Applications to Hospital Secretary within 7 days.

BROOK GENERAL HOSPITAL, Shooters Hill-road, Woolwich, S.E.18. HOUSE PHYSICIAN (Infectious Diseases Unit). This Unit provides excellent experience and is 1 of the Regional Centres for the treatment of bulbar poliomyelitis. 6 months appointment, salary £525 p.a., less £125 p.a. for residence.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

DREADNOUGHT SEAMEN'S HOSPITAL, Greenwich, S.E.10. Required, 1st October, 1954, SENIOR HOUSE OFFICER for Casualty and Receiving-room duties. Salary £745 p.a. Post recognised by Royal College of Surgeons.

Applications, stating age, qualifications and experience, with the names of 3 referees, to Group Secretary at above address on or before 24th September.

ELIZABETH GARRETT ANDERSON HOSPITAL, Euston-road, N.W.1. (ROYAL FREE HOSPITAL GROUP.) Applications are invited from pre-registration and registered Women medical practitioners for the post of FIRST HOUSE SURGEON, with charge of general surgical beds. Appointment for 6 months from 1st November, 1954. Salary according to Ministry of Health scale for House Officers.

Applications, with copies of 3 recent testimonials, should be sent to, the Secretary, Elizabeth Garrett Anderson Hospital, by 15th September, 1954.

ELIZABETH GARRETT ANDERSON HOSPITAL, Euston-road, N.W.1. (ROYAL FREE HOSPITAL GROUP.) Applications are invited from pre-registration and registered Women medical practitioners for the post of SECOND HOUSE PHYSICIAN. Appointment for 6 months from 1st November, 1954. Salary according to Ministry of Health scale for House Officers.

Applications, with copies of 3 recent testimonials, should be sent to, the Secretary, Elizabeth Garrett Anderson Hospital, by 15th September, 1954.

GUY'S-MAUDSLEY NEUROSURGICAL UNIT. Applications are invited for the post of SENIOR HOUSE OFFICER for 6 months commencing 1st October, 1954. The Unit, which is housed in the Maudsley Hospital, serves both Guy's Hospital and the Bethlem Royal Hospital and the Maudsley Hospital.

Applications to K. J. JOHNSON, House Governor and Secretary, Maudsley Hospital, Denmark-hill, London, S.E.5.

HACKNEY HOSPITAL, London, E.9. (General—844 Beds.) Applications from registered medical practitioners for the posts of HOUSE OFFICERS (casualty) (1 with additional duties in the Skin Department and 1 with additional duties in the E.N.T. Department), should be sent as soon as possible to the Group Secretary at the above address.

HAMPSTEAD GENERAL HOSPITAL, The Green, N.W.3. (ROYAL FREE HOSPITAL GROUP.) Applications are invited for the following pre-registration posts :—

HOUSE PHYSICIAN.
HOUSE SURGEON.

Both vacant 1st October, 1954, and tenable for a period of 6 months.

Application forms may be obtained from the Administrative Officer, to whom they should be returned, together with 3 recent testimonials, by 7th September, 1954.

HAMPSTEAD GENERAL HOSPITAL, The Green, N.W.3. (ROYAL FREE HOSPITAL GROUP.) Applications are invited from registered medical practitioners, for the post of RESIDENT CASUALTY OFFICER (graded as Senior House Officer). Salary £745 p.a. Vacant 1st October, 1954, tenable for a period of 6 months at the Main Outpatients Department, Bayham-street, N.W.1.

Application forms may be obtained from the Administrative Officer, to whom they should be returned, together with copies of 3 recent testimonials, by 7th September, 1954.

HIGHLANDS GENERAL HOSPITAL, Winchmore Hill, London, N.21. ANÆSTHETIST (House Officer grade), resident, required. 100 active surgical and orthopædic beds. Approximately 1200 operations annually.

Applications, with copies of 3 testimonials, to Hospital Secretary.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. 2 vacancies occur 1st November, 1954, for RESIDENT SURGICAL OFFICER. Appointments for 6 months, with prospect of renewal. Posts graded as Senior House Officer or Registrar, according to qualifications and experience. Previous surgical experience necessary.

Applications, stating age, qualifications with dates and previous appointments held, with copies of 3 testimonials, should reach the undersigned not later than 25th September.

THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

LONDON HOSPITAL, Whitechapel, E.1. Applications are invited for the post of SENIOR HOUSE OFFICER to the Department of Venereal Diseases.

Applications (6 copies), giving full particulars, together with 6 copies of 3 recent testimonials, should be received by the House Governor by 13th September, 1954.

PRINCE OF WALES'S GENERAL HOSPITAL, N.15. (219 Beds.) Applications are invited from registered medical practitioners for the following appointments, for a period of 6 months :—

SENIOR HOUSE OFFICER RESIDENT SENIOR HOUSE SURGEON, vacant 8th November, 1954.
RESIDENT SENIOR HOUSE SURGEON, third post, vacant 14th November, 1954.

Application forms from Secretary, Tottenham Group Hospital Management Committee, The Green, N.15, to be returned by 30th September, 1954.

LAMBETH HOSPITAL, Brook-drive, S.E.11. Lambeth GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited from pre-registration and registered medical practitioners for the post of RESIDENT HOUSE PHYSICIAN, vacant 1st October, 1954, at above Hospital.

Application forms from the Physician-Superintendent.

MOTHERS' HOSPITAL (Salvation Army). (110 Beds.) HACKNEY GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the 6 months appointment of RESIDENT OBSTETRIC HOUSE SURGEON (post-registration), vacant on 1st November, 1954. Post recognised for M.R.C.O.G.

Applications, together with copies of 3 testimonials, should be sent to the Secretary, Hackney Group Hospital Management Committee, Hackney Hospital, E.9, not later than 18th September, 1954.

NATIONAL HEART HOSPITAL, Westmoreland-street, London, W.1 (with which is associated the Institute of Cardiology). Applications are invited for the post of ASSISTANT RESIDENT MEDICAL OFFICER (Male). The appointment is for a period of 6 months from 1st October, 1954. The status of the post is that of a Senior House Officer and the salary is £745 p.a. in accordance with the terms and conditions of service of hospital medical staff.

Applications, with copies of 3 recent testimonials, should be sent to me not later than Saturday, 11th September, 1954.

ROBERT G. E. WHITNEY, Secretary to the Board.

NATIONAL HEART HOSPITAL, Maida Morston, Buck-INGHAM. (Country Branch of the National Heart Hospital.) Applications are invited for the post of RESIDENT MEDICAL OFFICER at the Hospital's Country branch. The appointment is for a period of 6 months from 1st October, 1954, but may be renewed for a further period not exceeding 6 months. The status of the post is that of a Senior House Officer, and the salary is in accordance with the terms and conditions of service of hospital medical staff. The holder will be expected to attend on 1 day weekly at the Hospital in Westmoreland-street.

Applications, with copies of 3 recent testimonials, should be sent to me at Westmoreland-street, London, W.1, not later than Saturday, 11th September, 1954.

ROBERT G. E. WHITNEY, Secretary to the Board.

NATIONAL HOSPITALS FOR NERVOUS DISEASES. Applications are invited from registered medical practitioners for the appointment of 2 ASSISTANT REGISTRARS (whole-time) to the Outpatients Department at The National Hospital, Queen-square, W.C.1. These posts carry the grade of Senior Registrar. The appointments will be for 1 year in the first instance.

Applications, giving the names of 3 referees, to be sent to the undersigned not later than 25th September, 1954.

H. EWART MITCHELL, Secretary.

The National Hospitals for Nervous Diseases,
W.C.1. Queen-square,

NEW END HOSPITAL, Hampstead, N.W.3. Registrar required for General Medical Unit of 85 Beds. Post vacant 1st October, 1954. The Hospital may be visited by direct appointment with the Surgeon-Superintendent.

Application forms obtainable from and returnable to Group Secretary, Archway Group Hospital Management Committee, 46, Cholmeley-park, N.6, by 11th September, 1954.

NORTH EAST METROPOLITAN REGIONAL HOS-PITAL BOARD.

1. E.N.T. REGISTRAR (non-resident), West Ham group of hospitals.

2. E.N.T. REGISTRAR (non-resident), Prince of Wales's and St. Ann's General Hospitals.

3. E.N.T. REGISTRAR (resident at Hackney Hospital), Hackney group of hospitals.

4. REGISTRAR in General Surgery (resident), Essex County Hospital, Colchester. Duties include some E.N.T. surgery. Post tenable for 18 months from 1st November, 1954, subject to review after first 12 months. A Senior Registrar will occupy post from 1st May, 1956, under joint training scheme. Recognised for F.R.C.S. but desirable that candidates should hold fellowship in surgery.

5. ORTHOPÆDIC REGISTRAR (resident), St. Andrew's Hospital, Billericay, Essex. (Duties mainly orthopædic and traumatic with some duties in General and Casualty Departments.)

6. CASUALTY REGISTRAR (resident), Oldchurch Hospital, Romford, Essex.

7. MEDICAL REGISTRAR (resident or non-resident), Oldchurch Hospital, Romford, Essex.

8. MEDICAL REGISTRAR (resident or non-resident but resident in hospital during duty periods if not living locally). St. Andrew's Hospital, Bow, E.3. Experience in chest diseases and/or pediatrics an advantage.

9. PÆDIATRIC REGISTRAR (non-resident), Queen Elizabeth Hospital for Children. (Duties include 1 visit a week to East End Maternity Hospital and 1 visit a week to a L.C.C. clinic.)

Appointments subject to review after 1 year.

Separate applications in duplicate, with 2 copies of 2 recent testimonials, to Secretary, 11A, Portland-place, W.1, by 18th September, 1954.

ST. MARY'S HOSPITAL FOR WOMEN AND CHILDREN, Upper-road, Plaistow, London, E.13. RESIDENT CASUALTY OFFICER/DEPUTY RESIDENT SURGICAL OFFICER (Registrar grade) required for 8 months commencing mid-October, 1954.

Applications, with copies of recent testimonials, to the Group Secretary, West Ham Group Hospital Management Committee, Stratford, London, E.13, by 15th September, 1954.

ST. STEPHEN'S HOSPITAL, Chelsea, S.W.10. Casualty OFFICER (with anæsthetic duties). Senior House Officer grade. Vacancy mid-September.

Applications, naming 2 referees, to Medical Superintendent, immediately.

PUTNEY HOSPITAL, Lower Common, S.W.15.

CASUALTY OFFICER AND FRACTURE HOUSE SURGEON (non-resident), House Officer grade, vacant 15th September, 1954.

CASUALTY OFFICER AND E.N.T. HOUSE SURGEON (non-resident), House Officer grade, vacant 29th September, 1954.

Apply immediately to Hospital Secretary, enclosing copies of 3 recent testimonials.

QUEEN CHARLOTTE'S MATERNITY HOSPITAL. QUEEN CHARLOTTE'S AND CHELSEA HOSPITALS. ANÆSTHETIST (Senior House Officer), resident, post tenable for 6 months from 1st October, 1954, in the first instance, for duties at both hospitals. Post recognised for the purposes of the F.F.A.R.C.S.

Applications to be sent to the Secretary to the Board of Governors by 14th September, 1954, on forms obtainable from 339, Goldhawk-road, London, W.6.

ROYAL FREE HOSPITAL. Applications are invited from registered Men and Women practitioners for the post of Locum RESIDENT ASSISTANT PATHOLOGIST at the above Hospital for the months of November and December. Duties to commence 1st November, 1954.

Application forms may be obtained from the Secretary to the Board of Governors, the Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 24th September, 1954.

ROYAL NATIONAL ORTHOPÆDIC HOSPITAL, BROCKLEY HILL, STANMORE, MIDDLESEX. Applications are invited for the posts of RESIDENT SENIOR HOUSE OFFICERS (2 vacancies) for a period of 6 months. 1 to commence duties on 6th November, and 1 on 27th November.

Applications to be received by 17th September. Forms of application can be obtained from the House Governor at 234, Great Portland-street, London, W.1.

ROYAL NATIONAL THROAT, NOSE AND EAR HOS-PITAL, Gray's Inn-road, W.C.1, and Golden-square, W.1, with which is associated the Institute of Laryngology and Otology (University of London). General Practitioner CLINICAL ASSISTANTS AND OUTPATIENT ASSISTANTS. These appointments give those engaged in general practice who are able to attend for 2 sessions weekly commencing in October, 1954, the opportunity of widening their clinical experience in the specialty. Remuneration under paragraph 10 (b) of the National Health Service terms and conditions of service at end of 3 months trainee period.

Further particulars may be obtained from the House Governor.

SOUTH LODGE HOSPITAL, World's End Lane, N.21. ENFIELD GROUP HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (first, second, or third post) resident. For general duties as directed by the Medical Superintendent. National Health Service salary plus £50 p.a. Vacant 1st November, 1954.

Applications with the names and addresses of 2 referees to the Medical Superintendent of the Hospital.

ST. CLEMENT'S HOSPITAL, London, E.3. Bow Group HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICERS (2) required for Psychiatric Unit consisting of 24 observation beds and 36 beds for treatment of neurosis and early psychoses. Unit run in conjunction with the London and Claybury Hospitals. Both posts recognised for D.P.M. Vacant beginning of October.

Apply to Group Secretary, Committee Offices, 2A, Bow-road, E.3, with names of 3 referees.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy on 1st November, 1954, for a RESIDENT ANÆSTHETIST (Registrar grade).

Full particulars, with form of application, which must be returned not later than Monday, 13th September, 1954, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy on 1st November, 1954, for a JUNIOR RESIDENT ANÆSTHETIST (Senior House Officer).

Full particulars, with form of application, which must be returned not later than Monday, 13th September, 1954, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy for a HOUSE PHYSICIAN (Senior House Officer) on 15th December, 1954.

Further particulars and form of application, which must be returned not later than Monday, 4th October, 1954, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

ABBOTS LANGLEY, HERTFORDSHIRE. LEAVESDEN HOSPITAL. SENIOR HOUSE OFFICER required at above Hospital for mental defectives (2240 Beds).

Applications to Physician-Superintendent.

ALTON GENERAL HOSPITAL. (121 Beds.) Winchester GROUP OF HOSPITALS. Applications are invited from registered medical practitioners for the post of RESIDENT HOUSE PHYSICIAN (Senior House Officer grade) with some experience of anæsthetics. Useful experience to be obtained in general medicine. The appointment is for 6 months in first instance. Vacant early November.

Applications, stating age, qualifications and experience, together with copies of 2 testimonials, to Group Secretary, Royal Hampshire County Hospital, Winchester.

ALTON GENERAL HOSPITAL. (121 Beds.) Winchester GROUP OF HOSPITALS. HOUSE SURGEON required to assist in steadily expanding surgical work including casualty at this Hospital which is being developed. Vacant early November.

Applications with copies of 2 testimonials, to be sent to the Group Secretary, Royal Hampshire County Hospital, Winchester.

ASHFORD (near), KENT. WILLESBOROUGH HOSPITAL. Applications are invited for the appointment of HOUSE PHYSICIAN at the above Hospital. Salary £425, £475, or £525 a year, less a deduction of £125 a year for residential emoluments.

Applications, stating age, qualifications and the names and addresses of 2 referees, to the Group Secretary, "Ash-Eton," Radnor Park West, Folkestone.

ASHFORD HOSPITAL, Ashford, Middlesex. Staines GROUP HOSPITAL MANAGEMENT COMMITTEE. RESIDENT HOUSE SURGEON (Male) required at above Hospital, for Orthopædic and Traumatic Unit. 6 months appointment, vacant on 26th October, 1954. Preference given to pre-registration candidates.

Applications, stating age qualifications and experience with copies of up to 3 recent testimonials, to be sent to Medical Director of Hospital.

AYLESBURY. ROYAL BUCKINGHAMSHIRE AND ASSOCIATED HOSPITALS MANAGEMENT COMMITTEE.

Stoke Mandeville Hospital (611 Beds)

SENIOR HOUSE OFFICER in the Rheumatism Research Centre, with additional duties in general medicine. New appointment.

Applications, with names of 2 referees, to the Administrative Officer.

HOUSE PHYSICIAN for Pædiatric Department. Post qualifies for D.C.H. Duties will include the care of children in Infectious Diseases Unit, Plastic Unit, and the Outpatient Department, Royal Bucks Hospital. Recognised pre-registration post. Applications from registered practitioners will be considered. Interview will be held on 23rd September. Post vacant from 7th October.

Apply with copies of 2 testimonials, to the Administrative Officer.

BARNSLEY. BECKETT HOSPITAL. (182 Beds.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time REGISTRAR (pathology) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 13th September, 1954, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

BATH HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from medical practitioners for the post of HOUSE PHYSICIAN at the Royal United Hospital and a second one at St. Martin's Hospital.

Applications, stating age, qualifications and experience, should be forwarded with 3 testimonials, to—

Manor Hospital, Bath. J. LAWRENCE MEARS, Secretary.

BATH HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of HOUSE SURGEON (orthopædic) which is a joint one between the adjacent Royal United and Bath and Wessex Orthopædic Hospitals. Post offers experience in "cold" orthopædics, including children, surgery of arthritis and traumatic surgery.

Applications, stating age, qualifications and experience, with 1 testimonial, should be forwarded to—

Manor Hospital, Bath. J. LAWRENCE MEARS, Secretary.

BATH HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from medical practitioners for post of HOUSE SURGEON (gynæcology and obstetrics) at the Bath group of hospitals. (Recognised for D.Obst.R.C.O.G.) Post vacant October.

Applications, stating age, qualifications and experience, with 3 testimonials, should be forwarded to—

Manor Hospital, Bath. J. LAWRENCE MEARS, Secretary.

BATH. ROYAL NATIONAL HOSPITAL FOR RHEUMATIC DISEASES. Applications invited from registered medical practitioners for post of HOUSE PHYSICIAN (Senior House Officer grade) at the above Hospital, attached to which is the Rheumatism Research Unit of South-Western and Oxford Regions. Hospital is recognised for part 2 of Diploma in Physical Medicine.

Applications, stating age, qualifications and experience, with 3 testimonials, should be forwarded to—

J. LAWRENCE MEARS, Secretary,
Bath Hospital Management Committee.
Manor Hospital, Bath.

BATH. ST. MARTIN'S HOSPITAL. Applications are invited from registered medical practitioners for the post of RESIDENT CASUALTY OFFICER (Senior House Officer grade) at above Hospital.

Applications, stating age, qualifications and experience, with 3 testimonials, should be forwarded to—

J. LAWRENCE MEARS, Secretary,
Bath Hospital Management Committee.
Manor Hospital, Bath.

BRENTWOOD, ESSEX. WARLEY HOSPITAL. Senior HOUSE OFFICER. The Hospital is situated within easy reach of London by main line electric service and bus. There are over 2000 Beds, and a wide experience of all types of mental disorders (including the neuroses) can be obtained. All modern treatments are carried out, including psychosurgery. Visiting Consultants in other specialties attend regularly. Teaching by senior staff and facilities for attending postgraduate courses are provided; also experience of outpatient clinics. Regular clinical meetings are held. The successful applicant will work under the direction of a Consultant Psychiatrist. Library, private bedroom, and individual sitting-room are provided. Indoor and outdoor recreational facilities. The post may be non-resident. Salary at the rate of £745 p.a., less a reasonable charge for residential emoluments.

Applications, stating age, experience and qualifications, should be sent to the Physician-Superintendent, with the names of 2 referees.

BARRY ACCIDENT AND SURGICAL HOSPITAL. CARDIFF HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER required immediately at above Hospital. Staffed by whole-time Consultant Surgeon and Senior Casualty Officer. Excellent experience given in general surgery.

Form of application from Group Secretary, Cardiff Hospita Management Committee, 44, Cathedral-road, Cardiff.

BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. ROYAL VICTORIA HOSPITAL, WESTBOURNE, HANTS. Applications are invited for the appointment of HOUSE SURGEON for E.N.T. and ophthalmic duties, vacant immediately. In addition to duties at the above Hospital, the successful candidate will be required to assist in the E.N.T. outpatient clinics at the Royal Victoria Hospital, Bournemouth, and Poole General Hospital. The appointment is recognised for the D.O. and D.L.O. Diplomas but not for pre-registration purposes.

Applications to the Deputy Hospital Secretary, Royal Victoria Hospital, Shelley-road, Bournemouth.

BOLTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE.

RESIDENT ANÆSTHETIST (Senior House Officer grade). Main duties at Bolton District General Hospital and Bolton Royal Infirmary. Vacant 21st October, tenable for 12 months and recognised for the D.A.

Bolton District General Hospital (604 Beds)

RESIDENT HOUSE PHYSICIAN for the Department of Pædiatrics. Not available to pre-registration candidates. Vacant 12th October, tenable for 6 months. Hospital recognised for D.C.H.

Applications, stating age, nationality, qualifications and experience, and the names of 2 referees, should be sent immediately to H. P. TRAVIS, Group Secretary, The Royal Infirmary, Bolton.

BEDFORD GENERAL HOSPITAL. (437 Beds.) North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. GENERAL SURGICAL REGISTRAR (resident) required at above Hospital. Hospital may be visited by direct appointment. Post vacant immediately.

Application forms obtainable from and returnable to, Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford, by 18th September, 1954.

BEDFORD GENERAL HOSPITAL. (437 Beds.) Locum RESIDENT GENERAL SURGICAL REGISTRAR required pending permanent appointment. Salary £16 per week.

Applications, stating age, nationality, qualifications, previous appointments together with copies of 2 recent testimonials, should be forwarded to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

BIRMINGHAM, 9. LITTLE BROMWICH HOSPITAL. Applications are invited for the post of HOUSE PHYSICIAN (Male or Female), vacant October, 1954. Recognised as pre-registration appointment.

Applications to the Physician-Superintendent.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

***1. Group 20 Hospital Management Committee, Stoney* Stanton-road, Coventry**

RESIDENT REGISTRAR in Infectious Diseases for Whitley Hospital, Coventry (143 Beds). Duties mainly with 90 infectious diseases beds; other units concerned with skin diseases and pulmonary tuberculosis. Liaison with Pædiatric Department. Self-contained flat available.

***2. South Worcestershire Hospital Management Committee,* Worcester Royal Infirmary, Worcester**

REGISTRAR (non-resident) in Pathology. Duties mainly at Worcester Royal Infirmary.

Application forms from Group Secretaries, to be returned before 20th September, 1954. Candidates may visit hospitals.

BIRMINGHAM. MONYHULL HALL HOSPITAL, King's HEATH, BIRMINGHAM, 14. BIRMINGHAM (NO. 8) HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of a JUNIOR HOSPITAL MEDICAL OFFICER (resident or non-resident). This mental deficiency hospital offers great experience in all branches of the investigation and training of mental defectives. In addition there are opportunities to gain experience with E.S.N. children and in child psychiatry at St. Francis Residential Special School, which is associated with the Hospital. There is a large, well-developed psychological department staffed by 3 clinical psychologists. The Hospital is recognised for the first year of the training for the D.P.M. Accommodation for a single person is available at a charge of £200 p.a.

Applications, giving full personal particulars, qualifications, and experience, together with the names and addresses of 2 referees, to be sent to the Medical Superintendent at the above Hospital within 2 weeks of the appearance of this advertisement.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE CHILDREN'S HOSPITAL. Applications are invited for the appointment of RESIDENT MEDICAL OFFICER in the grade of Senior House Officer, vacant 1st November, 1954, for 1 year.

Forms of application may be obtained from the House Governor, The Children's Hospital, Ladywood-road, Birmingham, 16, and should be returned not later than 20th September, 1954.

G. A. PHALP, Secretary to the Board of Governors.

BIRMINGHAM. THE SKIN HOSPITAL (Inpatients' Department), George-road, BIRMINGHAM, 15. Required, SENIOR HOUSE OFFICER or HOUSE OFFICER according to experience. Inpatients' Department is modern and well-equipped, providing facilities for study of skin diseases. Successful applicant will be required to assist Consultant at Outpatient clinics.

Applications, with copies of 2 recent testimonials, to the Secretary, Dudley Road Hospital, Birmingham, 18.

BIRMINGHAM, 29. SELLY OAK HOSPITAL. Applications are invited for the appointment of SENIOR HOUSE OFFICER (paediatrics). Recognised for D.C.H. Post tenable in the first instance for 6 months. Vacancy in October.

Applications to Medical Superintendent.

BRIGHTON. ROYAL ALEXANDRA HOSPITAL FOR SICK CHILDREN, Dyke-road, BRIGHTON, 1. (129 Beds and Cots.) SENIOR HOUSE OFFICER, vacant 1st October, 1954. Candidates should have experience in paediatrics (including surgery). Recognised for D.C.H.

Applications, stating usual particulars, with copies of 2 testimonials and names of 2 referees, to the Administrative Officer not later than 11th September, 1954.

BRIGHTON. SUSSEX EYE HOSPITAL. (56 Beds.) HOUSE SURGEON required at the above Hospital, vacant mid-September. Recognised for F.R.C.S. and D.O. Successful applicant will be considered for Senior House Officer post on completion of 6 months.

Applications, stating usual particulars and naming 2 referees, to the Administrative Officer.

BRIGHTON AND LEWES HOSPITAL MANAGEMENT COMMITTEE GROUP HOSPITALS. (78 Beds.) SENIOR HOUSE OFFICER (£670 p.a.) for duties in the E.N.T. Department of the above Group, vacant mid-September. Recognised for F.R.C.S., and D.L.O.

Applications, with details of experience, &c., together with the names of 2 referees, to be sent to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRADFORD CHILDREN'S HOSPITAL. Senior House OFFICER (Male or Female), vacant 22nd September. Recognised for D.C.H. Salary £745 p.a., less £150 p.a. residential emoluments.

Applications, stating age, nationality, qualifications and experience, with copy testimonials, to Secretary, Bradford Royal Infirmary.

BRADFORD ROYAL INFIRMARY.

HOUSE OFFICER (anæsthetics), vacant now. Recognised for D.A. and F.F.A.R.C.S. Opportunities for plastic and intrathoracic experience.

HOUSE SURGEON (general and urology), vacant 22nd September. Recognised for F.R.C.S. and pre-registration purposes.

Salary for either of above 2 posts £425–£525 p.a., less £125 p.a. residential emoluments.

Applications, stating age, experience, nationality and qualifications with copy testimonials, to Secretary.

BRADFORD ROYAL INFIRMARY. House Surgeon (general), vacant now. Recognised for F.R.C.S. and pre-registration purposes. Salary £425–£525 p.a., less £125 p.a. residential emoluments.

Applications, stating age, nationality, qualifications and experience with copy testimonials, to Secretary.

BRADFORD. ST. LUKE'S HOSPITAL. House Surgeon (general and plastic), vacant mid-September. Recognised for F.R.C.S. and pre-registration purposes. Salary £425–£525 p.a., less £125 p.a., residential emoluments.

Applications, stating age, nationality qualifications and experience with copy testimonials, to Secretary, Bradford Royal Infirmary.

BRADFORD. ST. LUKE'S HOSPITAL.

SENIOR HOUSE OFFICER (anæsthetics), vacant now. Salary £745 p.a., less £150 p.a. residential emoluments.

HOUSE OFFICER (anæsthetics), vacant now. Salary £425–£525 p.a., less £125 p.a. residential emoluments.

Opportunities for plastic and intrathoracic experience in both posts which are recognised for D.A. and F.F.A.R.C.S.

Applications, stating age, nationality, qualifications and experience, with copy testimonials, to Secretary, Bradford Royal Infirmary.

BRISTOL. COSSHAM/FRENCHAY HOSPITAL MANAGEMENT COMMITTEE. FRENCHAY HOSPITAL. (513 staffed beds, expanding.) Applications are invited for the post of SENIOR HOUSE OFFICER in the regional Neurosurgery Department. This post offers useful surgical experience and the opportunity of gaining a working knowledge of neurological diagnosis.

Applications to the Secretary, Frenchay Hospital, quoting "N.S.F." Names of 2 referees required.

BRISTOL. COSSHAM/FRENCHAY HOSPITAL MANAGEMENT COMMITTEE. FRENCHAY HOSPITAL. HOUSE SURGEON required to work in Plastic and Jaw Surgery Unit.

Applications, with full particulars, should be sent to the Group Secretary, Frenchay Hospital, Bristol.

BRISTOL. COSSHAM/FRENCHAY HOSPITAL MANAGEMENT COMMITTEE. FRENCHAY HOSPITAL. HOUSE OFFICER, Thoracic Surgery Department. House Surgeon required in the above Department, which is the regional thoracic surgery centre (120 Beds) for the South West.

Applications, with full particulars, should be addressed to the Group Secretary, Frenchay Hospital, Bristol, quoting "Thoracic."

BRISTOL. WINFORD ORTHOPÆDIC HOSPITAL. (230 Beds.) Applications are invited from registered medical practitioners to fill immediate vacancy for SENIOR HOUSE OFFICER. Appointment suitable for candidate reading for a higher grade qualification and is recognised for the F.R.C.S. Hospital is staffed by Consultants of teaching hospital.

Apply, stating age, qualifications and experience, with testimonials, to Secretary.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. BURY GENERAL HOSPITAL. SENIOR HOUSE OFFICER (surgical), resident or non-resident, at the above Hospital. Salary and conditions of service in accordance with national rules.

Applications should be made to—

H. WILKINSON, Esq., Group Secretary.

Bury General Hospital, Bury, Lancs.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. BURY GENERAL HOSPITAL. HOUSE OFFICER (pre-registration), surgery.

Apply, stating age, qualifications and names and addresses of 2 referees, to H. WILKINSON, Group Secretary.

Bury General Hospital, Bury, Lancs.

BURTON-ON-TRENT GENERAL INFIRMARY. (251 acute beds.) Applications are invited for the post of HOUSE SURGEON (obstetric and gynæcological). Post vacant mid-October. Designated for pre-registration service. The Hospital is recognised for the F.R.C.S.

Applications, with full details naming 2 referees, should be sent to the Secretary.

CAMBRIDGE. UNITED CAMBRIDGE HOSPITALS. RADIOLOGICAL REGISTRAR required for work in the Radiological Department at Addenbrooke's Hospital for 1 year in the first instance, reviewable annually. Applicants should have had some radiological experience but possession of D.M.R. not essential.

Apply, with full particulars and names of 3 referees, to Secretary, by 15th September.

CARDIFF HOSPITAL MANAGEMENT COMMITTEE. 2 SENIOR HOUSE OFFICERS required at Orthopædic Centre for South Wales at new Prince of Wales Orthopædic Hospital, Rhydlafar, near Cardiff, of 222 Beds (being extended to 292 Beds) plus 70 at country branch. Outpatients branch in Cardiff. Accommodation for single officers.

Application form from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

CARDIFF. ST. DAVID'S HOSPITAL. (656 Beds.) CARDIFF HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (resident or non-resident) required immediately for Geriatric Unit (200 Beds).

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

CARMARTHEN. WEST WALES GENERAL HOSPITAL. (188 Beds. Recognised by the Royal College of Surgeons and for pre-registration service.) WEST WALES HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT HOUSE OFFICER (surgical). Salary £425, £475, and £525 p.a., according to experience, less £125 p.a. for residential emoluments.

Applications, stating age, qualifications, experience and nationality, with names and addresses of 3 referees, to the Group Secretary, West Wales Hospital Management Committee, Glangwili, Carmarthen.

CHELMSFORD AND ESSEX HOSPITAL. Applications are invited for the resident post of CASUALTY OFFICER (Senior House Officer). It is recognised for the F.R.C.S. and offers excellent experience in the treatment of fractures and diagnosis of acute medical and surgical emergencies. Opportunity is given for Casualty Officer to follow up his cases in the wards and to obtain operating experience in major theatre under the guidance of the Consultants or the Resident Surgical Officer. Off-duty time is generous and the post is one likely to suit both an officer seeking a higher qualification in surgery or one intending General Practice. The vacancy will occur on 2nd October. Salary £745 p.a., with £130 deducted for residential emoluments.

Apply Secretary, Chelmsford Hospital Management Committee, Chelmsford and Essex Hospital, Chelmsford.

CHELMSFORD HOSPITALS. Applications are invited for the post of RESIDENT ANÆSTHETIST (Senior House Officer) to large surgical units, for a period of 12 months.

Applications, stating age, sex, qualifications and experience, with recent testimonials, should be sent to the Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford.

CHEPSTOW, MONMOUTHSHIRE. PLASTIC SURGERY, JAW INJURIES AND BURNS CENTRE, ST. LAWRENCE HOSPITAL. (100 plastic surgery, 50 orthopædic beds.) SENIOR HOUSE OFFICER in Plastic Surgery required towards end of September. Previous experience in specialty not essential. The successful candidate will receive a thorough training in plastic surgery and burns. Hospital intakes from most of Wales and provides extensive experience. A second Senior House Officer in Plastic Surgery was recently appointed and there is also a Senior House Officer in Orthopædics. Salary £745, less £150 board-residence.

Write, quoting 2 referees, to T. A. JONES, Group Secretary. 64, Cardiff-road, Newport, Mon.

COLCHESTER. ESSEX COUNTY HOSPITAL. (189 Beds.) Applications invited for post of SENIOR HOUSE OFFICER to Casualty and E.N.T. Departments. Post tenable for 6 months or 1 year. Recognised for F.R.C.S.

Applications, with copies of 3 testimonials, should be forwarded to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

CROYDON GENERAL HOSPITAL. (200 Beds.) Casualty OFFICER (Senior House Officer grade) for period of 6 months in first instance, commencing 1st October. Post is recognised for final F.R.C.S. examination.

Application forms obtainable from GEORGE A. PAINES, Secretary, Hospital Management Committee, General Hospital, Croydon, to be returned immediately.

DARLINGTON DISTRICT HOSPITAL MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER (mainly geriatrics). This is a joint post between East Haven (geriatrics) and Hundens Unit (a hospital of special departments) serving E.N.T., ophthalmic, infectious diseases, chest and chronic sick. Good experience with responsibility for suitable candidate. Post vacant September, is resident at Hundens Unit (single accommodation) and is for 4 years with option of reappointment. Salary £775–£50–£1075 p.a.

Applications should be sent forthwith, giving full particulars and 3 names for reference, to the Group Secretary, Darlington Memorial Hospital.

DERBY. DERBYSHIRE ROYAL INFIRMARY. House PHYSICIAN (pre-registration), vacant 1st October, 1954.

Apply, with copies of 2 testimonials, to Hospital Secretary.

DERBY. DERBYSHIRE ROYAL INFIRMARY. Senior HOUSE OFFICER (casualty), vacant immediately. Recognised for F.R.C.S.

Apply, with copies of 2 testimonials, to Hospital Secretary.

DERBY. DERBYSHIRE ROYAL INFIRMARY. (416 Beds.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT REGISTRAR (neurosurgery) required. Duties also at other hospitals in the Derby group. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 13th September, 1954, giving age, *nationality, qualifications, present and previous appointments* with dates, naming 3 referees.

DEWSBURY. THE GENERAL HOSPITAL, Moorlands-road. DEWSBURY, BATLEY AND MIRFIELD HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (surgery and casualty). Salary £745 p.a., less deductions for board and lodging.

Applications, stating age, qualifications, present and previous appointments, together with the names of 2 referees, should be sent to the Administrative Officer.

DONCASTER ROYAL INFIRMARY. Doncaster Hospital MANAGEMENT COMMITTEE. Applications are invited for the post of ORTHOPÆDIC HOUSE SURGEON in the grade of Senior House Officer. £145 p.a. deducted for residential emoluments.

Applications should be forwarded to the Secretary to the Committee, Doncaster Royal Infirmary.

DORCHESTER. DORSET COUNTY HOSPITAL. West DORSET GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. MEDICAL REGISTRAR required (Registrar grade) at above Hospital. Salary according to experience (£850 or £965 p.a.), with deduction of £160 p.a. if resident.

Application form which should be returned, duly completed by 18th September, 1954, from Group Secretary, West Dorset Hospital Management Committee, Damers-road, Dorchester.

DOUGLAS. NOBLE'S ISLE OF MAN HOSPITAL. (176 Beds.) Applications are invited from registered medical practitioners with previous hospital experience, preferably at a Teaching Hospital, for the post of SENIOR HOUSE SURGEON at this busy General Hospital. The senior of 4 House Officer posts. The post is now vacant, and is suitable for candidate seeking further clinical experience and opportunity for reading for higher qualification. Salary £745 p.a., with a deduction of £125 p.a. for board, lodging, &c., if resident.

Applications, giving relevant particulars, and copies of 2 recent testimonials, or names and addresses of 2 referees, should be forwarded to the Secretary, Noble's Isle of Man Hospital, Douglas.

DOVER. ROYAL VICTORIA HOSPITAL. Applications are invited for the post of HOUSE SURGEON at the above Hospital. The post is recognised by the Royal College of Surgeons. Salary £525 a year. A deduction of £125 a year will be made for residential emoluments.

Applications, stating age, qualifications, and the names and addresses of 2 referees, to the Group Secretary, "Ash-Eton," Radnor Park West, Folkestone.

DURHAM. DRYBURN HOSPITAL. (309 Beds.) Senior HOUSE OFFICER (general surgery) required. Post vacant 30th September, 1954. Recognised under F.R.C.S. regulations.

Applications, with names of 2 referees, to Group Secretary, Dryburn Hospital, Durham.

EDINBURGH. CHALMERS HOSPITAL. Applications are invited from registered or pre-registration medical practitioners for appointment of RESIDENT HOUSE SURGEON in the Gynæcological Annexe of the Hospital, for 6 months commencing 1st October, 1954, entailing responsibility for 24 gynæcological beds and 19 children's surgical beds.

Applications, stating age, qualifications and experience and names of 2 referees, to be sent immediately to Medical Superintendent, Edinburgh Central Hospitals, 18, Rillbank-terrace, Edinburgh, 9.

EDINBURGH. ROYAL HOSPITAL FOR SICK CHIL-DREN. Applications are invited from registered medical practitioners for appointment of RESIDENT HOUSE SURGEON, E.N.T. Department, for 6 months commencing 1st October, 1954. National Health Service scale.

Applications, stating age, qualifications and experience and names of 2 referees, to be sent immediately to Medical Superintendent, Edinburgh Central Hospitals, 18, Rillbank-Terrace, Edinburgh, 9.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. ENFIELD GROUP HOSPITAL MANAGEMENT COMMITTEE. Locum SENIOR HOUSE OFFICER for Casualty duties required from 27th September, 1954, to 9th October, 1954. Non-resident post. Hours: 9 A.M. — 5.30 P.M. Monday to Friday; 9 A.M. — 1 P.M. Saturday.

Applications, with the names and addresses of 2 referees, to the Secretary of the Management Committee at Chase Farm Hospital.

EPPING. ST. MARGARET'S HOSPITAL. (485 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (pathology) to fill an immediate vacancy. Salary on national scale, less deduction for board, lodging, &c. Busy department in large general hospital, with easy access to London. Some experience in pathological department desirable.

Applications, with copies of 2 recent testimonials, to reach the Group Secretary, Epping Group Hospital Management Committee, St. Margaret's Hospital, Epping, Essex, immediately.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. Locum CASUALTY REGISTRAR required at above Hospital from 6th September, 1954, for an indefinite period.

Apply immediately to Medical Director.

EDGWARE GENERAL HOSPITAL, Edgware, Middle-SEX. RESIDENT OBSTETRIC HOUSE SURGEON for above Hospital. Post vacant 26th September, 1954. Recognised for M.R.C.O.G. purposes.

Applications, stating age, qualifications, experience and enclosing copies of up to 3 recent testimonials, to Medical Director of Hospital by 11th September, 1954.

FARNBOROUGH HOSPITAL, *Farnborough, Kent.* (800 Beds.) HOUSE SURGEON required for 6 months from 12th October, 1954. Recognised for the F.R.C.S. Preference given to pre-registration candidates. Salary according to experience.

Apply, stating age, qualifications with dates, and experience and naming 3 referees, to the Administrative Officer by 10th September, 1954.

FARNBOROUGH HOSPITAL, Farnborough, Kent. (General—800 Beds.) RESIDENT SENIOR HOUSE OFFICER required for a busy E.N.T. Department with 4 specialist operating sessions, 5 outpatient clinics and a diagnostic hearing-aid centre. Recognised for D.L.O. and offers valuable experience in all aspects of E.N.T. work.

Apply, stating age, qualifications and experience, and naming 2 referees, to the Administrative Officer.

GLASGOW, N. STOBHILL GENERAL HOSPITAL. PSYCHIATRIC UNIT. HOUSE OFFICERS (resident). Male or Female, required now. (180 Beds.) 1300 admissions yearly. Acute treatable cases. Unit recognised for D.P.M. Salary £50 above standard rate.

Apply to Medical Superintendent.

GLASGOW, N. STOBHILL GENERAL HOSPITAL. Applications are invited now for the post of HOUSE OFFICER in the Phthisis Unit (32 Beds) and should be addressed to the Medical Superintendent.

GLASGOW, N. STOBHILL GENERAL HOSPITAL. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER in the acute Geriatric Unit (70 Beds—for assessment and rehabilitation), supervised by a Consultant Physician specialising in geriatrics. The appointment offers excellent clinical experience in the diagnosis and treatment of acute and other illnesses in the elderly, and will be for 2 years in the first instance.

Applications, stating age, qualifications and experience, with the names of 2 referees, should be sent to the Medical Superintendent.

GRIMSBY GENERAL HOSPITAL. (238 Beds.) Grimsby HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post (recognised for F.R.C.S. and D.L.O.) of PRE-REGISTRATION or SENIOR HOUSE OFFICER with duties in Surgical and E.N.T. Departments.

Applications, with names of 2 referees, to Hospital Secretary, Grimsby General Hospital.

GT. YARMOUTH AND GORLESTON GENERAL HOS-PITAL, DENE SIDE, GREAT YARMOUTH. HOUSE SURGEON (Male or Female) required. The Hospital is staffed by a Consultant General Surgeon and a Consultant E.N.T. Surgeon, and is regularly visited by Consultant staff from the Norfolk and Norwich Hospital. The post is a pre-registration post at a salary of £425, £475 or £525 p.a. according to experience, less £120 p.a. for residence. Membership of a Medical Defence Society is a condition of appointment.

Applications, stating age, qualifications and experience with names of 2 referees, to Hospital Secretary.

HALIFAX GENERAL HOSPITAL. (425 Beds.) Junior HOSPITAL MEDICAL OFFICER in Anæsthetics required. Opportunities for studying for D.A. Board-residence available.

Applications to Group Secretary, Royal Halifax Infirmary, Halifax.

HALIFAX. ROYAL HALIFAX INFIRMARY. (301 Beds.) HOUSE SURGEON (E.N.T. and ophthalmology) required. Post now vacant. Approved pre-registration appointment.

Applications to Group Secretary, Royal Halifax Infirmary, Halifax.

HALIFAX. ROYAL HALIFAX INFIRMARY. Obstetric HOUSE SURGEON required. Post vacant 1st October. Approved pre-registration appointment and recognised for D.Obst.R.C.O.G.

Applications to Group Secretary, Royal Halifax Infirmary, Halifax.

HAROLD WOOD HOSPITAL, Harold Wood, Essex. (415 Beds. Recognised for D.A. and F.F.A.R.C.S.) REGISTRAR (anæsthetics), resident, required from 1st September, 1954. Whole-time, initial period of 6 months, at main general and casualty hospital in Brentwood Group.

Apply to Hospital Secretary (Ingrebourne 2881).

HAROLD WOOD HOSPITAL, Harold Wood, Essex (near London). (415 Beds.) SENIOR HOUSE OFFICER (anæsthetics), resident. Main General and Casualty Hospital in group. Recognised for D.A. and F.F.A.R.C.S.

Apply, giving full details, to the Hospital Secretary (tel.: Ingrebourne 2881).

HOVE GENERAL HOSPITAL, Sussex. (75 Beds.) Senior HOUSE OFFICER (recognised for F.R.C.S.), vacant late September. Duties mainly those of Resident Surgical Officer.

Applications, stating particulars of qualifications, experience, &c., and naming 2 referees, to the Administrative Officer.

HERTFORD COUNTY HOSPITAL. (Situated 21 miles from London.) Applications are invited from registered medical practitioners for the appointment of a Whole-time Temporary REGISTRAR (surgical). To commence 17th September, 1954. Salary at the rate of £850–£965 p.a. according to service in the grade.

Applications, giving full details together with copies of recent testimonials or the names of referees, to Group Secretary, Hertford Hospital Management Committee, County Hospital, Hertford, Herts.

HULL. VICTORIA HOSPITAL FOR SICK CHILDREN, Park-street. HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. RESIDENT SENIOR HOUSE OFFICER required as from 15th September, 1954. *Duties mainly in Casualty Department.* Salary £745 p.a. Emoluments £155 p.a.

Send applications, with testimonials, to the Hospital Secretary.

HITCHIN, HERTFORDSHIRE. LISTER HOSPITAL. Applications are invited for the post of RESIDENT HOUSE PHYSICIAN, vacant 17th September, 1954. Recognised as pre-registration post.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to be sent to the Medical Administrator, Lister Hospital, Hitchin.

HITCHIN, HERTFORDSHIRE. LISTER HOSPITAL. Applications are invited for the post of RESIDENT HOUSE SURGEON, vacant 23rd September, 1954. Recognised as pre-registration post.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to be sent to the Medical Administrator, Lister Hospital, Hitchin.

HORNCHURCH. ST. GEORGE'S HOSPITAL. *Junior* HOSPITAL MEDICAL OFFICER (resident) required from 1st September, 1954, at this Hospital which accommodates 339 chronic sick patients. The post offers excellent geriatric experience.

Applications should be forwarded to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford, as soon as possible.

HEMEL HEMPSTEAD, HERTFORDSHIRE. WEST HERTS AND ST. PAUL'S HOSPITALS. Locum REGISTRAR in General Medicine required for indefinite period commencing 17th September, 1954.

Applications, with 2 names for reference, to the Secretary, West Herts Hospital.

INVERNESS HOSPITALS BOARD OF MANAGEMENT. ROYAL NORTHERN INFIRMARY, INVERNESS. HOUSE SURGEON (E.N.T. and eyes) required for 6 months. Whitley Council salary and conditions of service. Post recognised for pre-registration.

Applications with references to Medical Superintendent.

IPSWICH. ST. HELEN'S HOSPITAL. (100 Beds for infectious diseases, pulmonary tuberculosis and long-stay orthopædics. The area chest clinic is in the Hospital.) HOUSE PHYSICIAN required (post-registration appointment). Accommodation available for married man. The post also involves duties in the Pædiatric Department at the Borough General Hospital.

Applications to JOHN WILLIAMS, Group Secretary, Ipswich Group Hospital Management Committee, at East Suffolk and Ipswich Hospital, Ipswich.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR ANÆSTHETIC REGISTRAR (non-resident). Possession of F.F.A.R.C.S. desirable. The Anæsthetic Department comprises 3 teams, and every kind of surgical work is carried out except thoracic and neurosurgery.

Application forms obtainable from and returnable to Secretary, South West Middlesex Group Hospital Management Committee, West Middlesex Hospital, Isleworth, by 14th September, 1954.

KEIGHLEY AND DISTRICT VICTORIA HOSPITAL, KEIGHLEY, YORKSHIRE. (143 Beds.) RESIDENT HOUSE SURGEON (either sex) (general surgery, orthopædics, and E.N.T.) Post recognised under F.R.C.S. regulations. First, second, or third post, vacant now. Approved pre-registration appointment. Tenable for 6 months.

Applications, with full particulars as to age, nationality, qualifications, and experience, and copies of recent testimonials, to be sent to Group Secretary, St. John's Hospital, Fell-lane, Keighley.

LEAMINGTON SPA. WARNEFORD GENERAL HOS-PITAL. (207 Beds.) SOUTH WARWICKSHIRE HOSPITAL GROUP. Applications invited for the post of CASUALTY OFFICER (Senior House Officer), Male or Female, resident or non-resident. Post vacant and suitable for one reading for higher qualifications, affording contact with all specialist units in the Hospital.

Applications, with names and addresses of 3 referees, to Hospital Secretary.

LEAMINGTON SPA. WARNEFORD GENERAL HOS-PITAL. (207 Beds.) SOUTH WARWICKSHIRE HOSPITAL GROUP. Applications are invited for HOUSE OFFICER (anæsthetics). The post is recognised for D.A.

Applications as soon as possible to the Hospital Secretary.

LEICESTER ROYAL INFIRMARY. (507 Beds.) Sheffield REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT REGISTRAR (ophthalmology) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 13th September, 1954, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

LEICESTER ROYAL INFIRMARY. Applications are invited for the post of HOUSE SURGEON, vacant immediately. Recognised pre-registration post and for F.R.C.S.

Applications, stating age, and qualifications, with copies of testimonials, to Secretary, No. 1 Hospital Management Committee, 38A, East Bond-street, Leicester, forthwith.

LEICESTER (near). CARLTON HAYES HOSPITAL, NARBOROUGH, near LEICESTER. (851 Beds. Recognised for training for D.P.M.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time REGISTRAR (psychiatry) required. A house is available. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 13th September, 1954, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

LEEDS REGIONAL HOSPITAL BOARD. Short-term LOCUM TENENS appointments in the Registrar grade are constantly available at hospitals in the area of the Board, particularly in the specialties of anæsthetics, general medicine, general and orthopædic surgery, and psychiatry.

Interested practitioners, suitably experienced, should communicate with the Secretary, Joint Registrars Committee, Park-parade, Harrogate.

LEEDS REGIONAL HOSPITAL BOARD invites appli-cations for the appointment of REGISTRAR in Neurology (1 of 2 similar posts) for duties divided between the Department of Neurology at the General Infirmary at Leeds (20 Beds) and Pinderfields General Hospital, Wakefield (38 Beds).

Applications, stating age, qualifications and details of present and previous appointments with dates, together with the names and addresses of 3 referees, should be forwarded to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, not later *than 16th September, 1954.*

LEEDS REGIONAL HOSPITAL BOARD invites appli-cations for the following SENIOR REGISTRAR posts :—

Chest Diseases

Leeds Chest Clinic (non-resident). Offers excellent experience in all aspects of chest diseases. Over 5000 new cases annually. Access to associated beds at St. James's and St. George's Hospitals, Leeds, and at Middleton Hospital. Close functional association with the Thoracic Surgical Service.

Child Psychiatry

(*Training Post in Child Psychiatry.*) *The basic duties will be* 5 sessions in the University of Leeds, Department of Psychiatry (Children's Section) which is associated with the Leeds General Infirmary. Additional duties at Meanwood Park Colony, Leeds (mental deficiency) and/or St. James's Hospital, Leeds (adult neurosis). Residential accommodation available at Meanwood Park for single person. Candidates must hold the D.P.M. or equivalent qualification.

Applications, stating age, qualifications and details of appointments held showing dates, with names and addresses of 3 referees, to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, not later than 16th September, 1954.

LINCOLN. COUNTY HOSPITAL. (200 Beds.) Applica-tions are invited for the post of SENIOR HOUSE OFFICER in Surgery and E.N.T.

Applications, giving full particulars, should be addressed to—
R. W. HOWICK, Group Secretary.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. LIVERPOOL STANLEY HOSPITAL. Applications are invited for the following posts for the period 1st September, 1954, to 28th February, 1955 :—

ORTHOPÆDIC AND CASUALTY HOUSE SURGEON.
GYNÆCOLOGICAL HOUSE SURGEON.

The posts are open to both pre-registration and post-registration applicants.

Apply as soon as possible on form obtainable from the Secretary, The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. WALTON HOSPITAL. (1321 Beds.) A post as HOUSE PHYSICIAN (general medicine) will be vacant from 1st September, 1954. It is a recognised post for Pre-registration Service.

Applications, stating age, date of qualification, experience, and enclosing 2 copies of recent testimonials, to the Physician-Superintendent, Walton Hospital, Liverpool, 9.

LOWESTOFT AND NORTH SUFFOLK HOSPITAL, LOWESTOFT. (99 Beds.) Applications are invited for the appointment of SENIOR HOUSE SURGEON. Salary £745 p.a., less £150 for residential emoluments. The Hospital is staffed by Consultant General Surgeons and Visiting Consultants in all specialties from the Norfolk and Norwich Hospital.

Applications, stating age, qualifications and experience, with names of 2 referees, to Hospital Secretary, immediately.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the resident post of REGISTRAR in Gynæcology and Obstetrics, to the Blackpool and Fylde Group of hospitals, with main duties at Victoria Hospital, Blackpool, vacant 1st November, 1954. Post recognised for M.R.C.O.G.

Applications, together with names and addresses of 3 referees, should be sent to the Group Secretary, Blackpool and Fylde Hospital Management Committee, Victoria Hospital, Blackpool.

MANCHESTER REGIONAL HOSPITAL BOARD. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT REGISTRAR in Obstetrics and Gynæcology. The post is recognised for training for M.R.C.O.G. purposes and applicants should have had experience in obstetrics and gynæcology. The main duties will be at Withington Hospital which takes part in undergraduate teaching.

Application forms may be obtained from the Group Secretary, Withington Hospital, Manchester, 20, and should be returned immediately.

MANCHESTER REGIONAL HOSPITAL BOARD. Sal-FORD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for posts of NON-RESIDENT REGISTRAR, Neurosurgical Department at Salford Royal Hospital and the Royal Manchester Children's Hospital, and also for RESIDENT MEDICAL OFFICER (Registrar grade) at Salford Royal Hospital. In addition to adult work, the former post offers exceptional opportunities for experience in pædiatric neurosurgery.

Applications, with copies of 2 recent testimonials, to Group Secretary, Salford Royal Hospital, Salford, 3, by 10th September, 1954.

MANCHESTER REGIONAL HOSPITAL BOARD. ROCHDALE INFIRMARY. RESIDENT REGISTRAR in Surgery now vacant.

Apply, Group Secretary, Central Offices, Birch Hill Hospital, Rochdale.

MANCHESTER REGIONAL HOSPITAL BOARD. Bury AND ROCHDALE HOSPITAL GROUPS. RESIDENT REGISTRAR in Psychiatry now vacant.

Apply, Group Secretary, Central Offices, Birch Hill Hospital, Rochdale.

MANCHESTER REGIONAL HOSPITAL BOARD. REGISTRAR to assist at Bolton Chest Clinic and have clinical charge of small sanatorium of 59 Beds under the direction of the Consultant.

Applications, stating age, nationality, qualifications and experience, together with the names of 2 referees, should be sent immediately to the undersigned at the Royal Infirmary, Bolton. H. P. TRAVIS, Group Secretary,

Bolton and District Hospital Management Committee.

MANCHESTER REGIONAL HOSPITAL BOARD. Bury AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for REGISTRAR in Surgery at Bury General Hospital, the post falling vacant at the beginning of October.

Applications, together with the names of 2 referees, should be sent to H. WILKINSON, Group Secretary.

Bury General Hospital, Bury, Lancs.

MANCHESTER. ALTRINCHAM GENERAL HOSPITAL AND ANNEXE. (130 Beds.) SENIOR HOUSE OFFICER (surgical). This appointment affords excellent experience to suitably qualified candidates. Post recognised under F.R.C.S. regulations.

Applications to Group Secretary, North and Mid-Cheshire Hospital Management Committee, The Hospital, Sinderland-road, Altrincham, Cheshire.

MANCHESTER. BAGULEY HOSPITAL, Wythenshawe, MANCHESTER. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER required at the above Hospital. The appointment offers the opportunity to gain a wide experience in diagnosis of chest diseases and of the treatment both medical and surgical of respiratory tuberculosis, and will be limited to 4 years in the first instance.

Applications to be submitted to the Group Secretary, Withington Hospital, Manchester, 20, immediately.

MANCHESTER, 19. DUCHESS OF YORK HOSPITAL FOR BABIES. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN (Male or Female) required immediately for 6 months at the above Hospital which is associated with the Manchester University for teaching purposes.

Applications, with copies of 3 testimonials, to be sent to the Administrative Officer of the Hospital.

MANCHESTER. WYTHENSHAWE HOSPITAL. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of ASSISTANT SURGICAL OFFICER (Senior House Officer grade) at the above Hospital vacant on 1st October, 1954. Resident or non-resident. Post will provide experience in general surgery (adults and children) and gynæcology.

Applications to Group Secretary, Withington Hospital, Manchester, 20, immediately.

MAIDENHEAD HOSPITAL, St. Luke's-road, Maidenhead. RESIDENT SURGICAL REGISTRAR required at above Hospital. Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, Group Secretary, Windsor Group Hospital Management Committee, Alma-road, Windsor, by 12th September.

MAIDSTONE. KENT COUNTY OPHTHALMIC AND AURAL HOSPITAL. (113 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE SURGEON in the E.N.T. Department of the above Hospital. There are 55 E.N.T. beds and 6 specialist operating sessions each week. Valuable experience is available, and the post is recognised for the purpose of the F.R.C.S. and the D.L.O. Salary will be £745 a year, less £150 a year for residential emoluments.

Applications immediately to the Administrative Officer, Kent County Ophthalmic and Aural Hospital, Maidstone, Kent.

MAIDSTONE. KENT COUNTY OPHTHALMIC AND AURAL HOSPITAL. (113 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER in the Ophthalmic Department of the above Hospital. The Hospital is recognised by the Examining Boards for the F.R.C.S. and the D.O. Appointment will be for 12 months. Salary £745 a year, less £150 a year for residential emoluments. Post vacant 1st October, 1954.

Applications should be forwarded as soon as possible to the Administrative Officer, Kent County Ophthalmic and Aural Hospital, Church-street, Maidstone.

MAIDSTONE. OAKWOOD HOSPITAL. Required immediately for the above mental Hospital of 2200 Beds :—

Locum REGISTRAR. Salary £16 per week.

SENIOR HOUSE OFFICER. Salary £745 p.a.

Full residential accommodation is available for single Male officers the charge for which is at present £150 p.a. The Hospital which carries out all forms of treatment is conveniently situated enabling medical officers to attend D.P.M. and other courses in London. Outpatient clinics are held at local general hospitals.

Applications in writing, giving details and experience and the names of 2 persons to whom reference can be made, to be sent to the Medical Superintendent.

MITCHAM. CUMBERLAND HOSPITAL, Whitford-gardens, MITCHAM, SURREY. (100 Beds.) SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications invited for the post of RESIDENT MEDICAL OFFICER (Registrar) in Tuberculosis at the above Hospital. Duties also in Thoracic Unit, St. Helier Hospital. Experience in specialty essential.

Forms of application, returnable by 15th September, can be obtained from the Group Secretary, St. Helier Hospital, Carshalton, Surrey.

NEWCASTLE REGIONAL HOSPITAL BOARD.

South Shields District Hospital Management Committee

REGISTRAR ANÆSTHETIST, whole-time, resident or non-resident, single or married accommodation available. Appointment for 1 year in the first instance and may be renewed for a further period. Post recognised for F.F.A.R.C.S.

Newcastle upon Tyne Hospital Management Committee

REGISTRAR PHYSICIAN, whole-time, for Medical Clinic No. 1 at Newcastle General Hospital. Married accommodation may be available. Appointment for 1 year in the first instance and may be renewed for a further period.

North West Durham Hospital Management Committee

REGISTRAR PHYSICIAN for Medical Clinic No. 1 at Shotley Bridge General Hospital. This is a modern general hospital of 557 Beds dealing with acute medicine and surgery and has the following regional special centres attached to it —thoracic and cardiovascular, radiotherapy and plastic surgery. The appointment offers excellent facilities to anyone studying for a higher degree. The appointment is for 1 year in the first instance and may be renewed for a second year. Salary £850–£965 p.a.

Applications, together with names and addresses of referees (preferably), or testimonials, to a total of 3, to be sent to the Senior Administrative Medical Officer, "Blythswood South," Osborne-road, Newcastle upon Tyne, 2, within 14 days.

St. George's Hospital, Morpeth (1210 Beds)

REGISTRAR PSYCHIATRIST (whole-time), resident (single accommodation only available). Appointment for 1 year in the first instance and may be renewed for a further period. Arrangements can be made for the person appointed to take the necessary course of study for the University of Durham Diploma in Psychological Medicine.

St. Nicholas' Hospital, Gosforth, Newcastle upon Tyne (1190 Beds)

REGISTRAR PSYCHIATRIST (whole-time) resident (married accommodation available). Appointment for 1 year in the first instance and may be renewed for a further period. Arrangements can be made for the person appointed to take the necessary course of study for the University of Durham Diploma in Psychological Medicine. Salary £850–£965 p.a.

Applications, together with names and addresses of referees (preferably), or testimonials, to a total of 3, to be sent to the Regional Psychiatrist, "Blythswood South," Osborne-road, Newcastle upon Tyne, 2, within 14 days.

NEWTON ABBOT HOSPITAL. (General Section—65 Beds.) RESIDENT SENIOR HOUSE SURGEON (Male or Female) required immediately. Married quarters available.

Applications, stating qualifications, nationality, age, with copy testimonials, to be sent to the Group Secretary, Torquay District Hospital Management Committee, 62/64, East-street, Newton Abbot, S. Devon.

NORTH WEST DURHAM HOSPITAL MANAGEMENT COMMITTEE. SHOTLEY BRIDGE GENERAL HOSPITAL, SHOTLEY BRIDGE, CO. DURHAM; RICHARD MURRAY MATERNITY HOSPITAL, BLACKHILL, CO. DURHAM. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER (obstetrics and gynæcology). The appointment is for 1 year and the salary is £745 p.a., less emoluments valued at £150. Applicants must have been qualified not less than 1 year. The successful applicant will reside at Shotley Bridge General Hospital and will have duties in both Obstetrical and Gynæcological Departments, including clinics. The post is recognised for the M.R.C.O.G. for gynæcology.

Early application, accompanied by copies of 3 testimonials, should be made to the Group Secretary, A. LAWTHER, F.C.C.S., F.H.A., Shotley Bridge General Hospital, Shotley Bridge, co. Durham.

NORTH WEST METROPOLITAN REGIONAL HOS-PITAL BOARD. MEDICAL REGISTRAR required for the West Herts Hospital and St. Paul's Hospital, Hemel Hempstead. Hospitals may be visited by direct appointment. Post vacant 20th September, 1954.

Application forms obtainable from and returnable to, Secretary, West Herts Group Hospital Management Committee, 9, Rickmansworth-road, Watford, Herts, by not later than 10 days after the appearance of this advertisement.

NORTH WEST METROPOLITAN REGIONAL HOS-PITAL BOARD. Whole-time RESIDENT OBSTETRICAL AND GYNÆCOLOGICAL REGISTRAR required at Edgware General Hospital and Bushey Maternity Hospital. M.R.C.O.G. desirable. Department has 130 obstetrical and 40 gynæcological beds. Hospitals may be visited by direct appointment.

Application forms obtainable from and returnable to, Group Secretary, Edgware General Hospital, Edgware, Middlesex, by 14th September, 1954.

NORTHWOOD, MIDDLESEX. MOUNT VERNON HOSPITAL. (555 Beds.) NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required in the X-ray Diagnostic Department at above Hospital for 1 year in first instance.

Application forms obtainable from, and returnable to, the Secretary, Harefield and Northwood Group Hospital Management Committee, Mount Vernon Hospital, Northwood, Middlesex. Hospital may be visited by direct appointment.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited from registered general practitioners for the post of THIRD CASUALTY OFFICER (Senior House Officer grade). Salary (less £150 emoluments) and conditions of service in accordance with those laid down by the Ministry. Duties to commence as soon as possible. This post offers wide experience of casualty work. The Staff establishment requires only 1 night in 3 emergency work, and off duty permits time for study for higher examinations.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to—

General Hospital, Nottingham. HENRY M. STANLEY.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited from registered medical practitioners for 2 posts of SENIOR ORTHOPÆDIC AND FRACTURE HOUSE OFFICER (locum tenens considered). The posts offer exceptional experience in traumatic surgery. Duties to commence about 1st September, and about 1st October. Salary and conditions of service in accordance with Ministry regulations. If resident £150 deducted for emoluments.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to—

HENRY M. STANLEY, Group Secretary.

NOTTINGHAM. HIGHBURY HOSPITAL. Senior SURGICAL HOUSE OFFICER required at the above Hospital. Good opportunity for obtaining experience in all types of general surgery. Duties to commence on 1st September, 1954. Salary and conditions of service in accordance with the published conditions of the Ministry of Health. If resident £150 p.a. deducted for emoluments.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to—

HENRY M. STANLEY, Group Secretary.

Nottingham General Hospital.

NOTTINGHAM. MAPPERLEY HOSPITAL. (1067 Beds.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time REGISTRAR (psychiatry) required. Single accommodation available. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 13th September, 1954, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

NOTTINGHAM. CITY HOSPITAL. (804 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST (Senior House Officer), vacant immediately. The post is recognised for the D.A. and the F.F.A.R.C.S. and offers wide experience; this is a busy general hospital with Departments in General, Orthopædic, Thoracic, Cardiac, Plastic and Gynæcological Surgery.

Applications, stating age, nationality and qualifications, together with copies of not more than 3 testimonials, to be sent to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NORWICH. NORFOLK AND NORWICH HOSPITAL. (440 Beds.) EAST ANGLIAN REGIONAL HOSPITAL BOARD. SURGICAL REGISTRAR. Post provides wide experience and recognised for F.R.C.S. Appointment for 1 year, renewable for second year.

Applications, stating age, experience and names of 3 referees, to Secretary of Board, 117, Chesterton-road, Cambridge, by 13th September, 1954. Candidates invited to visit Hospital by direct arrangement with Hospital Management Committee Secretary at the Hospital.

ORPINGTON HOSPITAL, Orpington, Kent. Applications are invited for the post of RESIDENT CASUALTY OFFICER (Male) at Senior House Officer grade for above General Hospital (813 Beds). Post recognised for F.R.C.S.

Applications to the Physician-Superintendent.

OXFORD. LITTLEMORE (MENTAL) HOSPITAL. Applications invited for the post of SENIOR HOUSE OFFICER (Male or Female). Previous experience as House Surgeon or Physician essential. Previous psychiatric experience unnecessary. The Physician appointed will work primarily in the Insulin Therapy Clinic and with a Senior Consultant at outpatient clinics. There are ample facilities for postgraduate study in a teaching general hospital. Salary £745 p.a.

Applications to the Physician-Superintendent, Littlemore Hospital, near Oxford.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL. RESIDENT DENTAL HOUSE SURGEON, vacant immediately. Recognised for the Fellowship.

Applications, stating age, nationality, qualifications, and experience, with the names of 3 referees, to be sent to—

ARTHUR R. CASH, Group Secretary, Plymouth,
South Devon and East Cornwall General Hospital Group,
7, Nelson-gardens, Stoke, Plymouth.

READING AREA HOSPITALS. Applications are invited for post of SENIOR HOUSE OFFICER or JUNIOR HOUSE OFFICER (pathology). Previous experience in pathology desirable but not essential. Salary £745 or £525 p.a. respectively, less £125 board-residence.

Apply, stating age, qualifications with dates, nationality, present post, together with copies of recent testimonials, to Group Secretary, 3, Craven-road, Reading.

READING COMBINED HOSPITALS. Applications are invited from provisionally registered medical practitioners for 2 resident posts of JUNIOR HOUSE SURGEON (obstetrics) for above Hospitals, vacant 1st and 15th October, respectively. M.R.C.O.G. recognised, and tenable for 6 months.

Write, stating age, qualifications with dates, nationality, present post, with copy of recent testimonial, not later than 10th September, to Secretary, Royal Berkshire Hospital, Reading.

READING. ROYAL BERKSHIRE HOSPITAL. (403 Beds.) Applications are invited from registered medical practitioners for the appointment of JUNIOR HOUSE SURGEON (gynæcology), vacant 1st October. Post M.R.C.O.G. recognised. Tenable for 6 months. Salary £525 p.a., less £125 board-residence.

Write, stating age, qualifications with dates, nationality and present post, with copy of 1 recent testimonial, to the Secretary.

ROTHERHAM. DONCASTER GATE HOSPITAL. (155 Beds.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT MEDICAL REGISTRAR required with duties also at the Moorgate Hospital, Rotherham (355 Beds). Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 13th September, 1954, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

ROTHERHAM. OAKWOOD HALL SANATORIUM (100 Beds) AND THE CHEST CLINIC, ROTHERHAM. SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (chest diseases) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 13th September, 1954, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

ROCHDALE, LANCASHIRE. BIRCH HILL HOSPITAL. ROCHDALE AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (medicine), resident, required at above Hospital.

Apply to Group Secretary, Central Offices Birch Hill Hospital, Rochdale, Lancs, with names and addresses of 2 referees.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) SENIOR HOUSE OFFICER in Pathology required from end of September in this large general hospital containing well-equipped laboratory where excellent opportunities exist for gaining extensive experience.

Applications should be sent immediately to Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) SENIOR HOUSE OFFICER required in the Department of Ophthalmology from 22nd September, 1954.

Applications should be addressed immediately to the Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROMFORD, ESSEX. VICTORIA HOSPITAL. (99 Beds.) RESIDENT HOUSE SURGEON (Male) required, vacant middle September, 1954. (Post not approved for pre-registration purposes.)

Applications should be forwarded to the Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROMFORD. RUSH GREEN HOSPITAL. (301 Beds.) RESIDENT SENIOR HOUSE SURGEON required from 1st October, 1954. Recognised for F.R.C.S.

Applications should be forwarded immediately to Medical Superintendent, stating also names of 2 referees.

REDHILL. EAST SURREY HOSPITAL, Shrewsbury-road, REDHILL, SURREY, SENIOR HOUSE OFFICER (surgical) required at above Hospital.

Apply to the Hospital Secretary.

SCOTLAND. SOUTH-EASTERN REGIONAL HOS-PITAL BOARD. Applications are invited for an appointment of TRANSITIONAL SENIOR REGISTRAR in E.N.T. Surgery to the Edinburgh Northern Group of Hospitals. The main duties of the appointment will be in connection with in and outpatients in the Eastern and Western General Hospital, but will include certain duties in peripheral hospitals, primarily in the Scottish Border Counties. The salary for the post will be at the rate of £1400 p.a., the appointment being for a period of 1 year in the first instance. Applicants should have considerable experience in E.N.T. surgery, including the holding of a Senior Registrar appointment. The post is subject to the terms and conditions of the National Health Service.

Applications, giving particulars of age, qualifications, and previous experience, together with the names of 3 referees, should be submitted to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 2nd October, 1954.

SCOTLAND. SOUTH-EASTERN REGIONAL HOS-PITAL BOARD. Applications are invited for the appointment of SENIOR REGISTRAR in Orthopædic Surgery at the Royal Infirmary of Edinburgh. The appointment is subject to the terms and conditions of the National Health Service.

Applications, giving particulars of age, qualifications, and previous experience, together with the names of 3 referees, should be submitted to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, within 14 days.

SCOTLAND. SOUTH-EASTERN REGIONAL HOS-PITAL BOARD. Applications are invited for the post of SENIOR REGISTRAR in Ophthalmology at Bangour Hospital, Broxburn, West Lothian. The appointment is subject to the terms and conditions of the National Health Service.

Applications, giving particulars of age, qualifications and previous experience, together with the names of 3 referees, should be submitted to the Secretary, South-Eastern Regional Hospital Board, 11, Drumsheugh-gardens, Edinburgh, 3, by 2nd October, 1954.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance :—

REGISTRAR in Surgery based at the Victoria Infirmary, Glasgow.
REGISTRAR in Psychiatry based at Hawkhead Mental Hospital, Glasgow.
REGISTRAR in Surgery based at Stobhill Hospital, Glasgow.
REGISTRAR in Pædiatrics based at Stobhill Hospital, Glasgow.

These appointments are subject to the National Health Service (Scotland) superannuation regulations.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, by 18th September, 1954.

SHREWSBURY. ROYAL SALOP INFIRMARY/COP-THORNE HOSPITAL. (500 Beds.) Senior House Officer to work as CLINICAL PATHOLOGIST to Group Laboratory. Appointment tenable for 1 year, resident or non-resident, now vacant. (A Unit of the Public Health Laboratory service is housed in the same building.)

Applications to Group Secretary, Royal Salop Infirmary, Shrewsbury, naming 3 referees.

SHREWSBURY. EYE, EAR AND THROAT HOSPITAL. (70 Beds.) SENIOR HOUSE OFFICER (ophthalmic)—Eye Unit 35 Beds. Post recognised for the D.O.

Applications with copy testimonials to Group Secretary, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. SHELTON MENTAL HOSPITAL. (1000 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER. Hospital recognised for training for D.P.M.: all forms of treatment undertaken. Outpatient clinics.

Applications to Medical Superintendent, Shelton Hospital, Shrewsbury.

SHEFFIELD. CITY GENERAL HOSPITAL. (642 Beds.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT MEDICAL REGISTRAR required. Experience in neurology will be considered an advantage. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 13th September, 1954, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time SENIOR REGISTRAR in Psychiatry required for Middlewood Hospital, Sheffield (2089 Beds). House available. Appointment for 1 year in the first instance, reviewable annually. Opportunity for research and experience in the special branches of psychiatry available in the hospital area.

Application forms and further details obtainable from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 20th September, 1954.

SHEFFIELD REGIONAL HOSPITAL BOARD. Locum REGISTRAR (orthopædics) required at Doncaster Royal Infirmary. Remuneration at the rate of £16 per week with a deduction if resident.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, naming 2 referees.

SHEFFIELD REGIONAL HOSPITAL BOARD. Locum REGISTRAR (pathology) required at the Beckett Hospital, Barnsley, from 20th September for 1 month in first instance. Remuneration at the rate of £16 per week with a deduction if resident.

Apply Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, naming 2 referees.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. Applications invited for the following posts:—

(*a*) RESIDENT REGISTRAR or SENIOR HOUSE OFFICER in Anæsthetics. Post vacant. Grade according to qualifications and experience. The successful candidate may be required to work in any of the units of The United Sheffield Hospitals.

(*b*) NON-RESIDENT SENIOR HOUSE OFFICER in Pathology at the Royal Infirmary Unit. Post vacant.

Applications, stating age, qualifications and experience with the names of 3 referees, should be sent immediately:—

For post (*a*) Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield, 1.

For post (*b*) Superintendent, Royal Infirmary, Sheffield, 6.

Copy testimonials may be sent for post (*b*).

SIDCUP, KENT. QUEEN MARY'S HOSPITAL. Sidcup AND SWANLEY HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of CASUALTY OFFICER (Senior House Officer) to commence as soon as possible. Duties mainly surgical casualties and minor operations, with fracture work under general supervision of Orthopædic Surgeons. The post is recognised for F.R.C.S.

Applications, stating age, qualifications, and experience, with copies of recent testimonials, to the Secretary, Sidcup and Swanley Hospital Management Committee.

SOUTHAMPTON EYE HOSPITAL. (32 Beds. Recognised for the D.O.M.S.) RESIDENT SENIOR HOUSE OFFICER required from mid-September, 1954. Salary £745 p.a.

Applications, with copies of testimonials, should be forwarded as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Chest Diseases to fill a vacancy in the approved trainee establishment at Preston Hall Hospital, British Legion Village, Maidstone, Kent. The appointment will be for work in general tuberculosis and will provide experience with a major surgical unit and also at chest clinics. Candidates must have had good experience in general medicine and in the diagnosis and treatment of pulmonary tuberculosis in adults. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 18th September, 1954.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in E.N.T. Surgery to fill a vacancy in the approved trainee establishment at the South East Kent group of hospitals. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, 11, Portland-place, W.1, not later than 18th September, 1954.

SALISBURY GENERAL HOSPITAL. Salisbury Group HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON to the Orthopædic Department. This appointment, which is for 6 months, becomes vacant on 14th September, 1954.

Applications, stating age, nationality, and naming 2 referees, should be submitted to the Group Secretary, Odstock Hospital, Salisbury.

SCUNTHORPE. WAR MEMORIAL HOSPITAL. (267 Beds.) SCUNTHORPE HOSPITAL MANAGEMENT COMMITTEE. Vacancy for HOUSE SURGEON (Senior House Officer grade)—offering excellent experience in general surgery and gynæcology.

Applications, naming 2 referees, to Group Secretary.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (obstetrics and gynæcology) required. 2 posts vacant shortly—and September and mid-October (approximately). Pre-registration posts. Recognised for M.R.C.O.G. and D.Obst.R.C.O.G.

Detailed applications to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent, with copy testimonials as soon as possible.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. (845 Beds.) Recognised for D.A. and F.F.A.R.C.S.) STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER in Anæsthetics, vacant 1st October, 1954. Previous anæsthetic experience desirable, but not essential. The post offers experience in anæsthesia for all types of general surgery, thoracic and cardiac surgery, including an Obstetric Unit of 60 Beds. Staff includes a Senior Registrar, who shares in emergency duties.

Applications, with necessary details, and copy testimonials, to the Group Secretary, Stoke-on-Trent Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications invited for HOUSE OFFICER (general surgery) vacant now. Hospital recognised for F.R.C.S. examinations, and the post is recognised for experience during the pre-registration period.

Apply, with copy testimonials, stating age, nationality and full details of previous service, to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications invited for SENIOR HOUSE OFFICER (orthopædics). Post recognised for F.R.C.S.

Apply, stating age and nationality, together with details of previous service, to the Group Secretary, Stoke-on-Trent Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications invited for the post of SENIOR HOUSE OFFICER (ophthalmology). This is a self-contained department. Recognised for F.R.C.S. and D.O.

Applications to the Hospital Secretary.

ST. ALBANS CITY HOSPITAL, St. Albans, Herts. (382 Beds.) CASUALTY OFFICER (Registrar grade) required for the above Hospital. Post recognised for the F.R.C.S. regulations. Appointment tenable for 6 months, subject to review at end of this period.

Application forms are obtainable from and returnable to Group Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans, by 13th September, 1954.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. HOUSE PHYSICIAN required for post vacant 26th October. Salary on national scale. Preference given to persons seeking pre-registration House Officer post.

Applications, stating age, experience, and qualifications, with dates, together with copies of 2 testimonials, to Hospital Secretary, by 12th September.

TORQUAY. TORBAY HOSPITAL. Torquay District HOSPITAL MANAGEMENT COMMITTEE. RESIDENT SENIOR HOUSE OFFICER (surgery) required for mid-September, 1954. Post recognised for F.R.C.S. There is a complement of 5 Resident House Officers.

Applications, stating qualifications, nationality, age, with copy testimonials (and quoting Ref. F.955/45) to Group Secretary, Torquay District Hospital Management Committee, 62/64, East-street, Newton Abbot, S. Devon.

WORTHING GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTHLANDS HOSPITAL, SHOREHAM-BY-SEA, SUSSEX. Applications are invited for the post of ORTHOPÆDIC REGISTRAR to the Group with duties mainly at Southlands; there are also general surgical duties.

Forms of application are obtainable from the undersigned, who will be glad to furnish any further details regarding the post, and must be returned within 14 days from the appearance of this advertisement. A. V. OAKTON, Group Secretary.

WAKEFIELD. PINDERFIELDS GENERAL HOSPITAL. Locum SENIOR HOUSE OFFICER required for Orthopædic Department. Salary £13 a week. A charge at the rate of £155 p.a. will be made for full residential accommodation.

Apply to undersigned, giving full details of training, experience, &c., together with 2 names and addresses for reference.

W. BOWRING, Group Secretary.

Victoria Chambers, Wood-street, Wakefield.

WARWICK (near). KING EDWARD VII MEMORIAL SANATORIUM, HERTFORD HILL, near WARWICK. (Diseases of the chest—225 Beds.) SOUTH WARWICKSHIRE HOSPITAL GROUP (No. 14). JUNIOR HOSPITAL MEDICAL OFFICER (resident or non-resident). The Sanatorium is a modern one with a Thoracic Surgical Unit about to be opened.

Applications, with names and addresses of 3 referees, should be forwarded to the Medical Superintendent as soon as possible.

WARWICK HOSPITAL. (264 Beds.) Resident Orthopædic House Officer (Male or Female) required. Post vacant 13th September. Well-equipped Orthopædic and Fracture Unit of 52 Beds.

Applications, with 2 recent testimonials, to the Medical Superintendent, Warwick Hospital.

WEST BROMWICH AND DISTRICT GENERAL HOSPITAL. Edward-street, WEST BROMWICH. (144 Beds.) WEST BROMWICH AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE GROUP 18. Applications are invited for the post of HOUSE PHYSICIAN, vacant 1st October, 1954. Salary, terms and conditions in accordance with the Ministry of Health regulations. Post tenable for 6 months. Resident. Recognised for pre-registration scheme.

Applications, together with 3 recent testimonials, should be submitted to J. O. ROBINS, Group Secretary.

WESTON-SUPER-MARE GENERAL HOSPITAL. CASUALTY OFFICER (Senior House Officer grade) required for the above Hospital. Entirely new Casualty Department just completed. An unfurnished flat is available for a married man.

Applications, stating age, qualifications and experience, together with the names and addresses of 2 referees, should be addressed to the Group Secretary, Weston-super-Mare Hospital Management Committee.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL. (311 Beds.) SENIOR HOUSE OFFICER (orthopædics) required. Post recognised F.R.C.S. Wide experience available under Area Orthopædic team. Appointment for 6 months in first instance. Vacant 25th September.

Applications, with copies of 2 testimonials, to the Secretary.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL. (311 Beds.) SENIOR HOUSE OFFICER in the Pathological Department, vacant 1st October. Preferably resident. Duties will include training in the various branches of clinical pathology, especially hæmatology. Previous experience in clinical pathology desirable, but not essential.

Applications, with copies of 2 testimonials, to the Secretary.

WINDYGATES, FIFESHIRE. CAMERON I.D. HOSPITAL. REGISTRAR required for the above Hospital, which consists of 100 infectious diseases beds including 12 for treatment of tuberculous meningitis, and 30 chronic sick beds. Duties to commence 1st October.

Apply, with copies of 3 recent testimonials, to the Medical Superintendent, East Fife Hospitals Board of Management, 243A, High-street, Kirkcaldy.

WOLVERHAMPTON GROUP.

The Royal Hospital, Wolverhampton (an Associated Hospital of the University of Birmingham Medical School) SENIOR HOUSE OFFICER (Anæsthetist). Appointment recognised for D.A. and F.F.A.R.C.S. Vacant early October.

HOUSE OFFICER (Casualty Department), vacant now.

Applications, with copies of 3 recent testimonials to be sent to Group Secretary The Royal Hospital, Wolverhampton.

YORK A AND TADCASTER HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER required immediately for E.N.T. Department (30 Beds). Post recognised for D.L.O.

Applications, giving age, nationality, qualifications, experience, and names of 2 referees, to Secretary, Bootham Park, York.

YORKSHIRE. EAST RIDING HOSPITAL MANAGEMENT COMMITTEE.

East Riding General Hospital, Driffield, E. Yorks (269 Beds)

(*a*) HOUSE SURGEON (first, second, or third post), vacant now. Approved pre-registration post. General surgical duties. Recognised for F.R.C.S.

Broadgate (Mental) Hospital, Beverley, E. Yorks (650 Beds)

(*b*) SENIOR HOUSE PHYSICIAN, vacant now.

(*c*) HOUSE PHYSICIAN (first, second, or third post), vacant now.

Northfield Sanatorium, Driffield, E. Yorks (78 Beds)

(*d*) SENIOR HOUSE PHYSICIAN. Vacant end September. Offers experience all branches of tuberculosis within group, including surgery, M.M.R., and clinics. Times for study. Expatients welcome.

Salary for (*a*) and (*c*) is £425–£525, and for (*b*) and (*d*) £745. Fully qualified practitioners may apply for pre-registration post.

Detailed applications to Group Secretary, Westwood Hospital, Beverley, Yorks.

B.W.I. UNIVERSITY COLLEGE HOSPITAL OF THE WEST INDIES. Applications are invited from medically qualified practitioners for the post of JUNIOR RESIDENT PATHOLOGIST at the above-named teaching hospital which is approved by the London University. Previous experience in clinical pathology is not essential. Duties include supervising emergency calls on the Department of Pathology outside the usual working hours. The appointment will be for 1 year in the first instance, subject to renewal. Salary is payable at the rate of £775–£890 p.a., depending on experience and qualifications. Single accommodation is available, for which a deduction of £125 p.a. in respect of board, residence, &c., is made. Return first-class passage by sea will be paid for 1 person only.

Further information may be obtained from the Hospital Manager and Secretary, University College Hospital, Mona P.O., Jamaica, B.W.I., to whom applications, stating age, nationality, and details of qualifications and experience, together with 3 recent testimonials or names and addresses of 3 referees, should be sent by 30th September, 1954.

NEW YORK. ALBANY HOSPITAL, Albany, New York, U.S.A. INTERNSHIPS and RESIDENCIES available in 700-Bed general, private Albany Hospital, directly connected with Albany Medical College. Approved for all major specialties. Participating in exchange-visitor programme. Salary range $1320–$2220 annually in addition to laundry, uniforms and room. All appointments begin 1st July, 1955.

For further information apply to Medical Director.

NEW YORK. ALBANY HOSPITAL, Albany, New York U.S.A. NEUROLOGY RESIDENCIES available in 700-Bed, university-teaching, general hospital. Salary range $1620–$2220 annually, plus laundry, uniforms and room.

Address inquiries to Medical Director.

NEW YORK. ALBANY HOSPITAL, Albany, New York U.S.A. PSYCHIATRY RESIDENCIES available in 700-Bed, university-teaching, general hospital, with 60-Bed acute treatment Psychiatric Unit fully approved for 3 years training. Experience includes dynamically-oriented psychotherapy with children and adults, shock therapies and neurologic training. Salary range $1620–$4000 annually plus laundry, uniforms and room.

Address inquiries to Medical Director.

NEW YORK. NEW ROCHELLE HOSPITAL, New ROCHELLE, NEW YORK, U.S.A. (360-Bed general community hospital.) Approved by the Joint Commission on Accreditation of Hospitals. Also approved by the American College of Surgeons and American Medical Association for internship and residency training. Only graduates from approved university schools accepted. 2 INTERNSHIPS available for the term commencing 1st January, 1955. Stipend is $200 per month, plus complete maintenance. Passage back to England paid by Hospital after completion of 12-month internship.

Apply Superintendent.

MICHIGAN, U.S.A. OAKWOOD HOSPITAL, Dearborn, MICHIGAN. Applications are invited for 1 or 2-year General Practice RESIDENCY in new 230-Bed general hospital 10 miles from Detroit. Excellent facilities. Hospital approved for exchange-visitor programme. Salary begins at $275 per month.

Apply : Director.

Public Appointments

CIVIL SERVICE COMMISSIONERS invite applications from registered medical practitioners for the pensionable post of DEPUTY TREASURY MEDICAL ADVISER. Salary £2300 (London). Age at least 40 on 1st September, 1954. The duties are primarily connected with the part of the Treasury Medical Service which deals with the General Post Office and its complex industrial organisation. Candidates must have high professional qualifications and clinical experience. Experience of, or an interest in, problems of epidemiology and industrial medicine desirable.

Further particulars and application forms from the Secretary, Civil Service Commission, Burlington-gardens, London, W.1, quoting no. 4369/54. Application forms to be returned by 30th September, 1954.

HACKNEY. METROPOLITAN BOROUGH OF HACKNEY. Appointment of DEPUTY MEDICAL OFFICER OF HEALTH. The Borough Council invite applications for the above-mentioned post from registered medical practitioners with appropriate qualifications and experience. The salary, commencing at a figure to be fixed according to the experience and qualifications of the successful applicant, will be within the scale £1500 rising by 2 annual increments of £100 each and 1 of £50 to a maximum of £1750 p.a.

Form of application obtainable from me must be returned, duly completed, not later than 27th September, 1954.

DUDLEY SORRELL, Town Clerk.

Town Hall, Hackney, E.8, 23rd August, 1954.

WILTSHIRE COUNTY COUNCIL. Deputy County MEDICAL OFFICER OF HEALTH AND DEPUTY PRINCIPAL SCHOOL MEDICAL OFFICER. Applications for this appointment invited from registered medical practitioners possessing the D.P.H. and the necessary knowledge and experience of administration of Local Authority Health Services. Salary £1500–£100(2)–£50(1)–£1750 p.a. Travelling and subsistence allowances. Superannuable appointment, terminable by 3 months notice.

Applications (no forms are issued) with names and addresses of 3 referees, must reach me by 25th September, 1954.

P. A. SELBORNE STRINGER, Clerk of the County Council.

County Hall, Trowbridge.

HER MAJESTY'S COLONIAL SERVICE. British GUIANA. MEDICAL SUPERINTENDENT required for the Mental Hospital, Berbice. Under the direction of the Director of Medical Services, he will have charge of hospital, control of its staff, and supervision of its expenditure and revenue. Hospital accommodation is 597 Beds. Superintendent will medically supervise all patients and have whole-time assistance of a Medical Officer, not specially trained in treatment of mental diseases. Superintendent will also be in charge of psychiatric clinic held monthly in Georgetown. Appointment on permanent basis with pension (non-contributory) at age of 55. Doctors in the National Health Service may resign from the National Health Service but retain their superannuation rights during their time in the Colonial Service (up to 6 years) and receive a resettlement grant of 20% of the aggregate of their Colonial salary on leaving the Colonial Service. Total emoluments of £1562 10s.–£1762 10s. a year made up as follows : salary scale £1000–£1200 p.a. ; non-pensionable allowance of £300 p.a. in lieu of consultation fees ; pensionable specialist allowance of £200 p.a. ; and a temporary (non-pensionable) cost-of-living allowance of £62 10s. p.a. Private practice is not permitted. Pension is earned at the rate of 1/600th of final pensionable emoluments for each completed month of service. Income-tax at local rates. Free unfurnished quarters are provided. Local leave permissible and generous home leave granted after each tour of 2–3 years. On appointment free passages provided for officer, wife, and children under 18 years, not exceeding 5 persons in all. Free passages on leave provided for officer and wife only. Candidates must possess medical qualifications registrable in the United Kingdom, hold a Diploma in Psychological Medicine, and have had at least 2 years experience in a mental hospital.

Application forms from Director of Recruitment (Colonial Service), Colonial Office, Sanctuary Buildings, Great Smith-street, London, S.W.1. (quoting reference BCD.117/30/05).

HER MAJESTY'S COLONIAL SERVICE. Mauritius. An ASSISTANT RADIOLOGIST is required in the Medical Department of Mauritius to perform radiological work, therapeutic and diagnostic, and such other duties as required by the Director of Medical Services. Appointment will be on contract for 3 years with gratuity on satisfactory completion of service. Salary scale ranges from Rs.10,020 to Rs.19,020 (£751 10s.–*£1426 10s.*) *a year. In addition a temporary non-pensionable* cost-of-living allowance is payable amounting to 12% on salary up to Rs.12,000 (£900) a year and 9% on all salary over *Rs.12,000 (£900) a year.* Candidates in the National Health Service may resign from the National Health Service but retain their superannuation rights (up to a limit of 6 years) during their time in the Colonial Service, and receive a resettlement grant of 20% of the aggregate of their Colonial salary on leaving the Colonial Service. Quarters are not provided, but officers who have not been allocated Government houses will be reimbursed any difference between approved rent paid for a private house (subject to a maximum of Rs.300 (£22 10s.) a month) and the 10% of salary they would normally pay for a Government house. For this purpose, officers residing in hotels or boarding houses will be regarded as paying half the board and lodging charge for themselves and their wives in respect of rent. Income-tax at local rates. Free passages in both directions are provided for officer, wife, and children, not exceeding 5 persons in all. Generous home leave is granted after tour. Candidates must have medical qualifications registrable by the General Medical Council in the United Kingdom, and experience in both radiodiagnosis and radiotherapy would be an added recommendation.

Application forms can be obtained from the Director of Recruitment (Colonial Service), Colonial Office, Sanctuary Buildings, Great Smith-street, London, S.W.1 (quoting reference BCD.117/52/016).

SHEFFIELD EDUCATION COMMITTEE. Applications are invited from duly qualified medical practitioners (Men and Women) for appointment as SCHOOL MEDICAL OFFICER. Special consideration will be given to the applications of candidates who have had experience in the treatment of children. Possession of the D.P.H. or D.C.H. qualification will be an advantage. Salary scale to be in accordance with the Whitley Councils for the Health Services (Great Britain) Medical Council, Committee "C." Superannuable post. Subject to satisfactory medical examination.

Application forms and particulars of the appointment may be obtained from the Director of Education, Education Office, P.O. Box 67, Leopold-street, Sheffield, 1, and should be returned not later than 25th September, 1954.

BIRMINGHAM. CITY OF BIRMINGHAM. Public HEALTH DEPARTMENT. Applications are invited for the appointment of a Part-time SPECIALIST ANÆSTHETIST to work in the Maternity and Child Welfare Dental Service. Duties will be concerned with the giving of anæsthetics for dental extractions to expectant and nursing mothers and young children under the age of 5 years. Preference will be given to applicants who hold the D.A. or similar higher qualifications. Remuneration will be at the rate of 4 guineas per session.

Applications, which should include details of age, qualifications and experience, together with the names of 3 referees, should be submitted to the Medical Officer of Health, Public Health Department, Congreve-street, Birmingham, 3, not later than the 18th September, 1954.

THE MEDICAL SERVICE OF THE ROYAL NAVY

VACANCIES FOR MEDICAL OFFICERS

Candidates are invited, for Short Service Commissions of 4 years, on termination of which a gratuity of £600 (tax free) is payable. Ample opportunity is granted for transfer to Permanent Commissions on completion of 1 year's total service. Officers so transferred are paid instead a grant of £1500 (taxable).

All entrants are required to be British subjects whose parents are British subjects, to be medically fit, and to pass an interview.

Full particulars from the Admiralty Medical Department, Queen Anne's Mansions, St. James's Park, London, S.W.1.

General Practice

For an Executive Council post (England and Wales) apply on form E.C.16A *obtainable from the council. Mark envelope "Vacancy."*

GRIMSBY, LINCOLNSHIRE. Applications are invited for a VACANCY (chiefly urban) which will arise at the beginning of December, 1954, as the result of the retirement (owing to ill health) of a single-handed practitioner. List at present approximately 2400. Present spacious practice accommodation available. Apply on Form E.C.16A before 14th September, 1954, to the undersigned from whom further details may be obtained.

K. PRIDGEON, Clerk of the Grimsby Executive Council.
(First Floor), 91, Cleethorpe-road, Grimsby.

Hospital Services : Non-Medical Appointments

ROCHDALE AND DISTRICT HOSPITAL MANAGE-MENT COMMITTEE. Applications are invited for the whole-time post of BIOCHEMIST (senior grade) to the Rochdale Group of Hospitals. The successful applicant will be required to work under the Consultant Pathologist and to perform biochemical estimations and examinations for the hospitals and clinics of the Group. Further details may be obtained from the Group Pathologist, Birch Hill Hospital, Rochdale. Commencing salary dependent on qualifications and experience, rising to a maximum of £1080 p.a.

Applications, together with names and addresses of 3 referees, should be forwarded to the Group Secretary, Central Offices, Birch Hill Hospital, Rochdale, Lancashire, as soon as possible.

Appointment : Too Late for Classification

POPLAR HOSPITAL, East India Dock-road, E.14. (120 Beds.) Required, HOUSE SURGEON (pre-registration post). *Duties* include inpatient, outpatient, and casualty work. Recognised for F.R.C.S. Vacant now.

Applications, stating age, nationality and qualifications, to *the Secretary.*

Miscellaneous

To non-professional posts the Notification of Vacancies Order 1952 applies.

Research Manager. A well-known and old established company, manufacturing ethical medicinal preparations, invite applications for the position of Research Manager to direct a team of Organic Chemists, Pharmacologists, Biochemists and Bacteriologists and to coördinate their work with clinical and other investigations necessary for the assessment of new drugs. Qualifications required are a degree in 1 of the major sciences, experience in pharmacology and proven experience in directing research. Preference will be given to candidates with previous experience in a similar post. Commencing salary will be dependent on qualifications and experience but will not be less than £2000 p.a. The position carries high status in the Company and offers good prospects. Contributory pension scheme.—Applications should be marked "Confidential" and addressed to: Address, No. 958, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Medical Officer required for Middle East by large oil company; preference for those with overseas experience and some knowledge of tropical work. Age about 35 and preferably single. Emoluments total over £1800 p.a.; paid home leave after 2 years; pension fund.—Write, quoting No. 379 to BOX No. 7956, c/o CHARLES BARKER & SONS LTD., 31, Budge-row, London, E.C.4.

Oil Company in the British West Indies invites applica-tions from registered medical practitioners for the position of Assistant Medical Officer. Duties will include dispensary and general hospital work. Candidates should be between 30 and 35 with good general experience. Basic salary from £1500 p.a., plus allowances and pension scheme. Apply, with brief particulars to—Address, No. 965, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Required, Radiologist prepared to help in Internal Medicine and Anæsthesia in group practice in East Canadian Province. Office and X ray and possible residence available. Hospital appointment in radiology open. Excellent financial opportunity. Reply, giving full details and references.—Address, No. 963. THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Physician willing to assist in General Practice required for prosperous and expanding European practice in town in Kenya highlands with modern well-equipped hospital. Principal visiting U.K. will interview applicants.—Write: 22, Randalls-road, Leatherhead, Surrey.

Locum Tenens offered by M.R.C.S. for work in London, W.5.—Address, No. 964, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

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Consulting-rooms, full and part time, and Houses in the medical area.—ELGOOD & Co., 1, Bentinck-street, W.1 (WELbeck 8974).

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"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimen of urine and £1 1s. fee. Hæmatology, Biochemistry. Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

Applicants for posts requiring testimonials copied or duplicated should communicate with MANTON SECRETARIAL SERVICE, LTD., 98, Victoria-street, S.W.1 (Phone: VICtoria 0141), who are specialists in this kind of work.

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